INDEX NUMBER
Section 1

Paid Circulation, 25,711

LIBRARY
JUL 14 1952
MANHATTAN
KANSAS

The New England Journal of Medicine

FORMERLY THE BOSTON MEDICAL AND SURGICAL JOURNAL — *Established 1828*

VOLUME 246 JUNE 26, 1952 NUMBER 26

Ureteral Complications and Alterations of Ureteral Tonus in Regional Ileitis . . . 993
Milton H. Redish

Fungous Disease in Man Acquired from Cattle and Horses (Due to *Trichophyton faviforme*) 996
Otis Field Jillson and William R. Buckley

A Comparison of the Duration of Action of Various Long-Acting ACTH Preparations in Human Subjects 1000
William Q. Wolfson and Stefan S. Fajans

Chiari's Disease — Hepatic-Vein Thrombosis . 1004
Anthony P. Caputi and Thomas A. Warthin

Medical Progress: Objectives and Limitations of Orthodontic Therapy 1007
Lennard T. Swanson

Massachusetts Department of Public Health 1024

Miscellany 1024

Medical Intelligence: Acute Calcific Tendinitis and "Frozen Shoulder": Their Treatment with ACTH. 1012
T. B. Quigley and Albert E. Renold

Case Records of the Massachusetts General Hospital 1015

Editorials:

Cui Bono 1021

The Forsyth Dental Infirmary for Children . . . 1022

Immunization in Relation to Poliomyelitis . . . 1023

Medical Society of London 1023

Correspondence 1024

Notices 1024

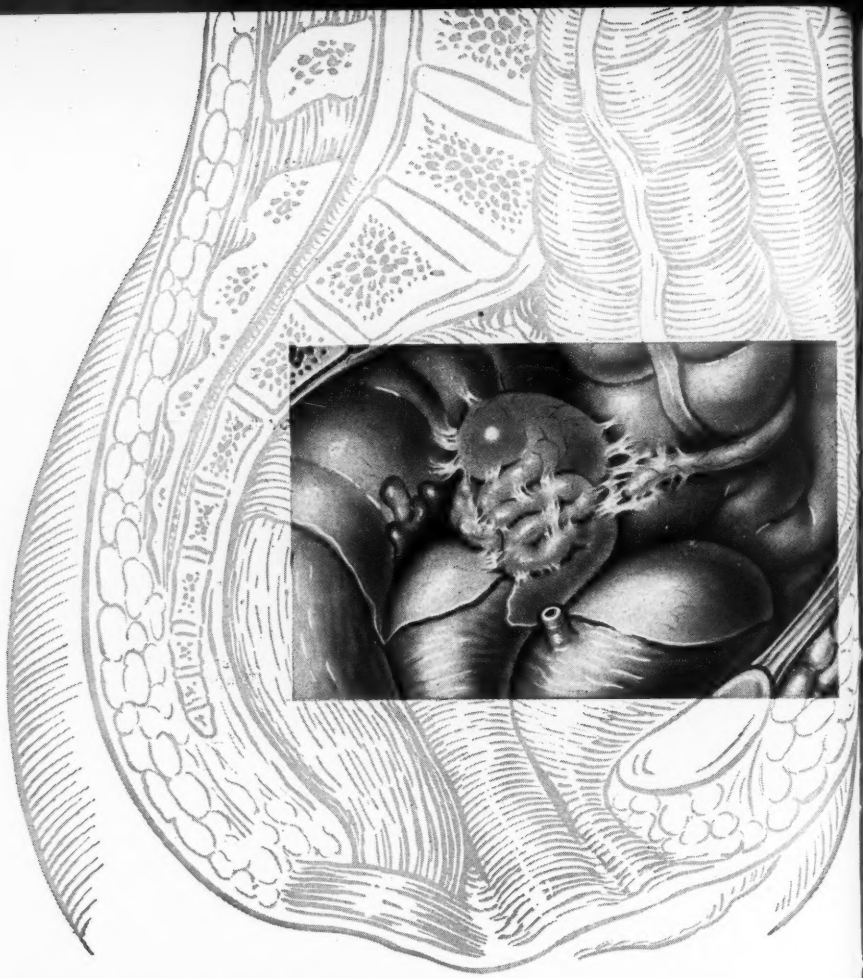
Entered as second-class matter, November 16, 1932, at the post office at Boston, Massachusetts, under the Act of March 3, 1879.

New! Leopold's Physical Diagnosis

This is certainly one of the most useful *new books* on the physical diagnosis of the entire body to be published in recent years. It was written by Dr. Simon Leopold, who helped to revise the final edition of the classic Norris and Landis' "Diseases of the Chest and the Principles of Physical Diagnosis." The author has succeeded well in presenting the basic methods of diagnosis (inspection, palpation, percussion and auscultation) and combining them with the latest principles of acoustic and x-ray interpretation. Special emphasis is always placed on the mechanistic causes of signs and symptoms.
Dr. Leopold has also borrowed many superb photographs from "Norris and Landis" which you will certainly want to own.

By Simon S. Leopold, M.D., Associate Professor of Clinical Medicine and Director of the Teaching of Physical Diagnosis, the University of Pennsylvania Medical School; Chief of the Thoracic Clinic, Hospital of the University of Pennsylvania. 430 pages, 6" x 9", with 390 illustrations, 19 in color. $7.50. *New*

W. B. Saunders COMPANY
WEST WASHINGTON SQUARE, PHILADELPHIA 5



rapid response

with **Chloromycetin®**

APPLIED SCIENCE LIBRARY
JUN 14 '52
MANHATTAN
KANSAS STATE

in pelvic inflammatory disease.....

CHLOROMYCETIN produces prompt clinical response in the mixed infections commonly found in pelvic inflammatory disease. "In mixed infection [pelvic cellulitis and abscess] CHLOROMYCETIN appears to be superior to penicillin, streptomycin or sulfadiazine."[1]

"The clinical response to chloramphenicol consisted of marked symptomatic improvement, usually within 48 hours....

"Women who had large pelvic abscesses were treated so effectively with chloramphenicol that posterior colpotomy, with drainage of the abscess, was not necessary in effecting a rapid cure in any of our patients who were treated with this antibiotic from the start."[2]

CHLOROMYCETIN (chloramphenicol, Parke-Davis) is supplied in a variety of forms including:

CHLOROMYCETIN	Kapseals®, 250 mg., bottles of 16 and 100.
CHLOROMYCETIN	Capsules, 100 mg., bottles of 25 and 100.
CHLOROMYCETIN	Capsules, 50 mg., bottles of 25 and 100.
CHLOROMYCETIN	Ophthalmic Ointment, 1%, ⅛-ounce collapsible tubes.
CHLOROMYCETIN	Ophthalmic, 25 mg. dry powder for solution, individual vials with droppers.

1. Greene, G. G.: Kentucky M. J. *50*:8, 1952.
2. Stevenson, C. S., et al.: Am. J. Obst. & Gynec. *61*:498, 1951.

MEDICAMENTA VERA · P D & CO.

Parke, Davis & Company
DETROIT, MICHIGAN

NEW HAMPSHIRE MEDICAL SOCIETY

OFFICERS FOR 1951–1952

PRESIDENT: B. READ LEWIN, Claremont
PRESIDENT-ELECT: JOSEPH N. FRIBORG, Manchester
VICE-PRESIDENT: RAYMOND H. MARCOTTE, Nashua

COUNCILORS: Douglass W. Walker, Belknap County, 1953; Ralph W. Tuttle, Carroll County, 1952; Albert C. Johnston, Cheshire County, 1954; William M. Bronson, Coos County, 1952; Arthur W. Burnham, Grafton County, 1953; Norman W. Crisp, Hillsborough County, 1955; Charles H. Parsons, Merrimack County, 1955; Willard C. Montgomery, Rockingham County, 1956; Samuel J. King, Strafford County, 1956; John H. Munro, Sullivan County, 1954.

SECRETARY AND TREASURER: DEERING G. SMITH, Nashua
SPEAKER OF THE HOUSE OF DELEGATES: LOUIS C. THEOBALD, Exeter
VICE-SPEAKER, HOUSE OF DELEGATES: FREDERICK S. GRAY, Portsmouth

TRUSTEES: Ralph W. Tuttle, Wolfeboro, 1952; James W. Jameson, Concord, 1953; George C. Wilkins, Manchester, 1954.

NECROLOGIST: Ralph W. Tuttle, Wolfeboro.

DELEGATE TO THE AMERICAN MEDICAL ASSOCIATION: Deering G. Smith, Nashua.

ALTERNATE DELEGATE, AMERICAN MEDICAL ASSOCIATION: Howard P. Sawyer, Brookfield.

COMMITTEES

EXECUTIVE: Immediate Past President, Harris E. Powers, Manchester; President; President-Elect; Vice-President; Secretary and Treasurer; Speaker of the House of Delegates; Vice-Speaker of the House of Delegates.

ADVISORY COMMITTEE ON JURISPRUDENCE: Earl J. Gage, Belknap County; Howard P. Sawyer, Carroll County; Robert W. Holmes, Cheshire County; William M. Bronson, Coos County; M. Dawson Tyson, Grafton County; David W. Parker, Hillsborough County; Robert O. Blood, Merrimack County; Lawrence R. Hazzard, Rockingham County; Edward G. Marcotte, Strafford County; B. Read Lewin, Sullivan County.

AMENDMENTS TO THE CONSTITUTION AND BY-LAWS: Henry Saltonstall, Exeter; John H. Branson, Concord; Albert E. Barcomb, Rochester.

CONTROL OF CANCER: George C. Wilkins, Manchester; Ralph E. Miller, Hanover; Walter H. Lacey, Keene; John R. Perley, Laconia; James W. Jameson, Concord; George F. Dwinell, Manchester.

COUNCIL OF THE NEW ENGLAND STATE MEDICAL SOCIETIES: B. Read Lewin, Claremont; Joseph N. Friborg, Manchester; Deering G. Smith, Nashua.

EMERGENCY MEDICAL SERVICE: Daniel J. Sullivan, Nashua; Clarence E. Dunbar, Manchester; Joseph M. McCarthy, Concord; John B. Holyoke, Hanover; Percy Grigg, Rochester; Reginald F. DeWitt, Plymouth.

INDUSTRIAL HEALTH: Robert Flanders, Manchester; George S. Baldry, Reeds Ferry; Francis H. Nolin, Claremont; Charles F. Keeley, Claremont; Robert W. Holmes, Keene; Robert Kaschub, Berlin; Daniel F. McCooey, Dover; John C. Eckels, Laconia; John H. Kennard, Manchester; Timothy F. Rock, Nashua; Charles I. Umpa, Nashua; Joseph D. Whelan, Manchester.

INFANT AND CHILD HEALTH: Douglass W. Walker, Laconia; Ursula G. Sanders, Concord; Thomas B. Walker, Concord.

MATERNAL HEALTH AND OBSTETRICS: Robert O. Blood, Concord; Robert N. Lord, Manchester; Frederick S. Gray, Portsmouth.

MEDICAL EDUCATION AND HOSPITALS: John P. Bowler, Hanover; James A. Ferguson, Lancaster; Edna Walck, Dover.

MEDICAL ECONOMICS: Norman W. Crisp, Nashua; James D. Skillen, Claremont; Marjorie A. Parsons, Colebrook.

MENTAL HYGIENE: John L. Smalldon, Concord; John E. McKenna, Hanover; Simon Stone, Manchester.

NOMINATIONS: Harris E. Powers, Manchester; Reginald K. House, Hanover; William H. Gifford, Colebrook; Roger P. Brassard, Laconia; Leroy S. Ford, Keene.

PROGRAMS: B. Read Lewin, Claremont; Deering G. Smith, Nashua; Jackson W. Wright, 2 years, Hanover; Warren H. Butterfield, 2 years, Concord; Howard P. Sawyer, 1 year, Brookfield.

PUBLIC HEALTH: Thomas M. Dudley, Concord; S. Gerard Griffin, Portsmouth; Robert C. Storrs, Hanover.

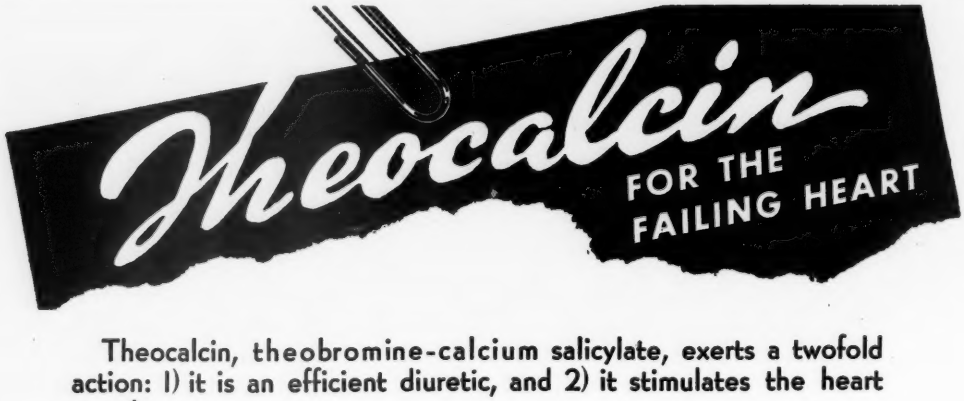
RURAL MEDICAL SERVICE: Robert I. Hinkley, Groveton; Alfred D. Mihachik, Northwood Narrows; Israel A. Dinerman, Canaan.

TUBERCULOSIS: Robert B. Kerr, Manchester; Francis J. Kasheta, Glencliff; John D. Spring, Nashua.

HOUSE OF DELEGATES

THE IMMEDIATE PAST-PRESIDENT, Harris E. Powers, Manchester, ex-officio.
PRESIDENT, ex-officio.
PRESIDENT ELECT, ex-officio.
VICE-PRESIDENT, ex-officio.
SECRETARY AND TREASURER, ex-officio.
BELKNAP COUNTY: Roger P. Brassard, Laconia; Reginald F. DeWitt, Plymouth.
CARROLL COUNTY: Howard P. Sawyer, Brookfield; Francis J. C. Dube, Center Ossipee.
CHESHIRE COUNTY: Samuel E. Paul, Troy; Louvane A. Fox, Keene.
COOS COUNTY: William H. Gifford, Colebrook; Marjorie Parsons, Colebrook.
GRAFTON COUNTY: James G. Bogle, Littleton; Reginald K. House, Hanover; Leslie K. Sycamore, Hanover; Leslie E. McKinlay, North Haverhill.
HILLSBOROUGH COUNTY: Claire G. Cayward, New Ipswich; Stanley C. Lewkowicz, Nashua; Raymond H. Marcotte, Nashua; Frank F. Flagg, Nashua; Edward D. Hagerty, Manchester; Robert Flanders, Manchester.
MERRIMACK COUNTY: Warren H. Butterfield, Concord; Edward V. Putnam, Warner; William D. Penhale, Concord; Francis Brown, Henniker.
ROCKINGHAM COUNTY: Frederick S. Gray, Portsmouth; Louis C. Theobald Exeter; Henry Saltonstall, Exeter.
STRAFFORD COUNTY: Edna Walck, Dover; Thomas F. Reid, Dover.
SULLIVAN COUNTY: Donald C. Moriarty, Newport; B. Read Lewin, Claremont.

The 1952 combined session of the New Hampshire and Vermont State Medical Societies will be held September 7-9, at the Mount Washington Hotel, Bretton Woods, New Hampshire



Theocalcin, theobromine-calcium salicylate, exerts a twofold action: 1) it is an efficient diuretic, and 2) it stimulates the heart muscle.

For most cases of congestive heart failure, a dose of 1 or 2 Theocalcin Tablets given 3 times a day will suffice. Theocalcin is well tolerated and not likely to cause nausea or headache.

Theocalcin Tablets, 7½ grains (0.5 Gm.) each. Powder, for prescription compounding.

Bilhuber-Knoll Corp. Orange, N. J.

The New England
Journal of Medicine

Copyright, 1952, by the Massachusetts Medical Society

Volume 246 JUNE 26, 1952 Number 26

URETERAL COMPLICATIONS AND ALTERATIONS OF URETERAL TONUS IN REGIONAL ILEITIS*

MILTON H. REDISH, M.D.†

BROOKLYN, NEW YORK

THE occurrence of extravesical urinary-tract complications of regional ileitis has not been adequately appreciated by urologists and gastroenterologists. It is the purpose of this report to call attention to these diagnostic possibilities and to illustrate with several cases the clinical and roentgenographic pictures that may be due to the secondary retroperitoneal spread of the inflammatory process.

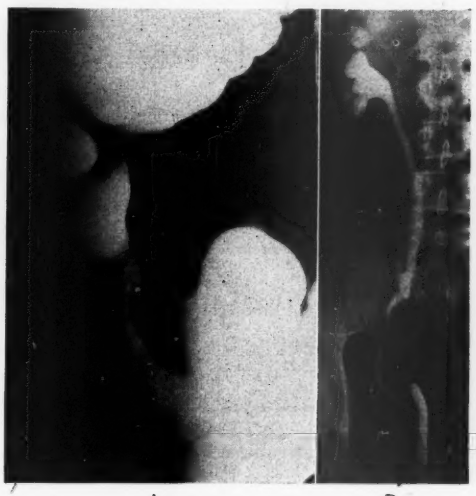
Of specific interest is the fact that the presenting complaints may be almost entirely urinary whereas the gastrointestinal symptoms are minimal. This was true of the first reported case.[1] On the other hand, the urinary-tract complication may be completely asymptomatic and may be detected only when sought by urologic technics.

The tendency to fistula formation often complicated by abscess is well known in regional ileitis and requires little emphasis. In the present consideration, retroperitoneal abscess is specifically excluded. This complication is obviously secondary to fistulous tract formation and has been well documented in the past.[2, 3] However, in none of the cases to be described was this tendency the primary cause of the ureteral involvement. Interestingly enough, it is the inflammation of the involved segment of bowel that compromises the ureter by retroperitoneal spread and gives rise first to hydroureter and secondly to either calyectasia or hydronephrosis.

The following case demonstrates the primary urinary-tract (ureteral) symptomatology with minimal gastrointestinal complaint.

CASE 1 (Reg. 1243). A 32-year-old veteran, was admitted on June 13, 1950, with a 3-week history of marked dysuria and acute right-flank pain radiating to the right testis. In 1944 there had first occurred a similar complaint, which was short-lived, and although he had then been hospitalized, no specific diagnosis was established. In the following year there gradually developed intermittent low-grade fever, mild abdominal cramps and "loose bowels." These symptoms recurred from time to time and in 1948, on the basis of a small-bowel series, a diagnosis of regional ileitis was established. The symptoms, however, were so mild as not to require therapy.

The pertinent physical findings on the current admission included a temperature of 102°F., localized deep right-lower-quadrant tenderness, a positive right psoas sign and clubbing of the fingers. The urine contained no protein, concentrated well (1.024) and was microscopically negative.



A B

FIGURE 1. *Roentgenograms in Case 1.*
A = *Classic string sign.* B = *Hydroureter and hydronephrosis.*

A small-intestine x-ray series revealed a typical string sign (Fig. 1*A*) in the distal ileum. Retrograde urography showed a right double ureter joining at the sacroiliac level. The right renal pelvis was likewise reduplicated, and the ureters as well as the renal pelves were considerably dilated (Fig. 1*B*).

From the time of admission until surgical exploration on July 11, 1950, the patient had intermittent severe right-loin pain and fever. At operation a cartilaginous-like mass was found encompassing the distal common ureter just below the point of fusion of the two ureters. Frozen section disclosed inflammatory tissue. A T-tube was implanted in the ureter and the peritoneum was entered. A large, edematous, acutely inflamed segment of the distal ileum was found tightly bound down to the posterior peritoneum; this inflammatory reaction, by extending posteriorly, had involved the common right ureter in the obstructive process.

Although no surgery other than the exploration and biopsy was performed, a ureterocutaneous fistula developed postoperatively. Finally a nephroureterectomy was performed

*From the Gastroenterology Section, Department of Medicine, Brooklyn Veterans Administration Hospital.

Reviewed by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions of the author are the result of his own study and do not reflect the opinion and policy of the Veterans Administration.

†Clinical instructor in medicine, New York University College of Medicine; chief of gastroenterology, Brooklyn Veterans Administration Hospital.

in September, 1950, and subsequently, in November, 1950, an ileotransverse colostomy, with excision of the involved ileum. Wound healing was slow but complete. One year later there occurred a deep fissure-in-ano that still drains from time to time.

The second case demonstrates a comparable but not so severe urinary-tract disturbance and came to our attention shortly after the first one. Gastrointestinal involvement here was extensive and the diarrheal symptoms severe.

CASE 2 (Reg. 4926). A 62-year-old man was admitted with a history of sudden right-flank pain of 1 day's duration. In 1941 he had a gastric resection for peptic ulcer. He was well until June, 1950, when symptoms of partial intestinal obstruction appeared that after 4 days' observation indicated operative intervention. The clinical report from the Carson C. Peck Memorial Hospital (where the surgery was performed) described many "skip" areas of inflammation of the jejunum and ileum, several areas of partial small-bowel obstruction due to the strangulating effect of adhesion formation and large succulent mesenteric nodes. One hundred and five cm. of ileum and jejunum was removed and continuity was reestablished by an enteroenteric anastomosis. Microscopical examination of the tissues showed regional enteritis.

The postoperative course was uneventful for the next 3 months, when an explosive diarrhea occurred, with a weight loss of about 25 lb. This cleared spontaneously after 3 weeks. The patient subsequently had no complaints of consequence until the acute symptoms of right nephroureteral involvement brought him to the Brooklyn Veterans Administration Hospital.

There was marked right-lower-quadrant tenderness. No fever or leukocytosis was present, but the urine showed many clumps of pus cells. At cystoscopy the urine obtained from the right ureter showed this side to be the site of the inflammation, and a hemolytic micrococcus was cultured. On aureomycin therapy the inflammation subsided. The retrograde urogram revealed a markedly dilated right ureter and a mild degree of hydronephrosis. X-ray films of the small intestine showed distortion of the terminal ileal mucosal pattern, persistent narrowing and fixation of this area. The subsequent clinical course was uneventful, and follow-up retrograde studies were normal.

Case 2 is unusual not only from the point of view of the extensive small-bowel involvement but also because of the patient's age. Although ileitis has been described in the older age groups, its clinical detection in the later decades of life is indeed quite rare.

On the basis of these experiences, all subsequently admitted patients with ileitis were subjected to intravenous pyelography for screening purposes. Four cases of ureteral involvement out of a series of 22, none of which had any urinary complaints, were detected.

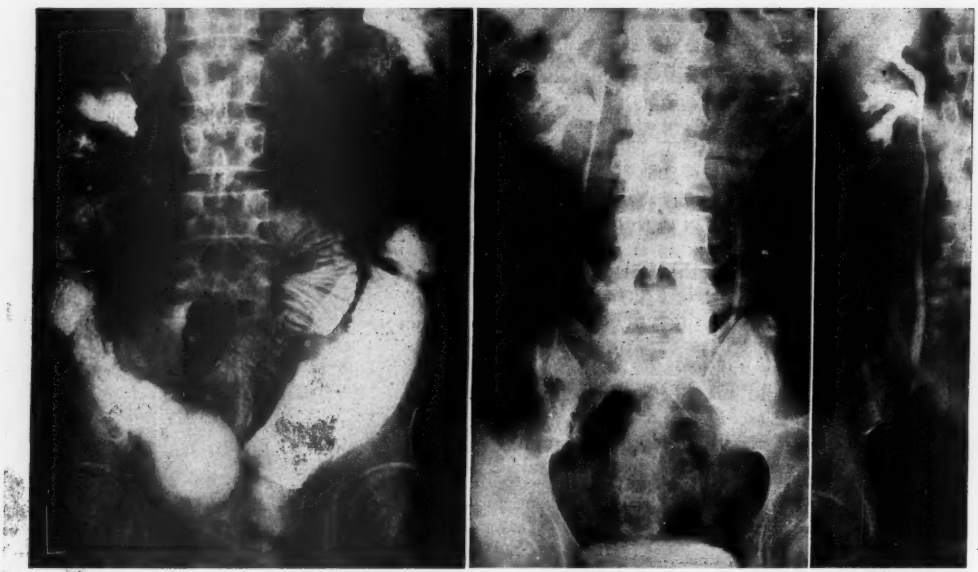


FIGURE 2. *Roentgenograms in Case 3.*
A = *Markedly disorganized pattern of small intestine.* B = *Dilated right ureter (arrow), medial displacement and positive Hutter sign*[6]; C = *Retrograde study of right side, showing mild hydronephrosis and point of constriction at pelvic brim.*

CASE 3 (Reg. 4353). A 32-year-old veteran was admitted on January 22, 1951, with an 8-year history of intermittent diarrhea and abdominal cramps. In 1945 a diagnosis of ileitis was established at operation. Early in 1950 the diarrheal symptoms became severe — up to 12 loose, watery stools per day. He was admitted to the Brooklyn Veterans Administration Hospital in January, 1951.

He showed considerable weight loss. The abdomen was markedly distended, and giant peristaltic rushes, from left to right, were readily visible. Small-bowel studies (Fig. 2*A*) showed involvement from the fourth part of the duodenum to the terminal ileum, with many skip areas alternating with zones of involvement.

The intravenous pyelogram showed medial displacement and dilatation of the right ureter (Fig. 2*B*). Retrograde studies highlighted a stricture of the ureter at the level of the lumbosacral joint (Fig. 2*C*). The urine examination and culture were negative.

At operation, the small bowel showed evidence of acute inflammation in four zones — two in the jejunum and two in the ileum. The lower jejunal and the upper ileal zones of involvement were adherent to each other and also to the right posterior wall of the abdomen at the level of the ureteral stricture. The inflammatory reaction at this site was extremely firm and had evidently penetrated posteriorly. A by-passing jejuno-transverse colostomy was performed. Of additional interest was the finding of a chronic peptic ulcer on the anterior surface of the pyloroduodenal junction.

The postoperative course was smooth and uneventful. Subsequent follow-up urograms showed a restitution to normal.

FIGURE 3. *Roentgenogram in Case 4, Showing Ureteral Dilatation.*

CASE 4 (Reg. 4282). A 28-year-old veteran was admitted on January 16, 1951. His gastrointestinal symptoms, — intermittent bouts of diarrhea, — dated back to 1943. In 1949 an ileostomy was performed at a private hospital. One month after discharge from that institution he had a massive intestinal hemorrhage. A colectomy was performed, leaving only the rectosigmoid. Admission to the Brooklyn Veterans Administration Hospital was sought because of symptoms of partial intestinal obstruction. Attempts to obtain information about the findings at the time of ileostomy and colectomy were unsuccessful.

Proctoscopy revealed only pallor and questionable granularity of the rectal mucosa. Retrograde barium studies (via the ileostomy) demonstrated the roentgenographic picture of regional ileitis. Pyelography showed bilateral ureteral dilatation, more marked on the right than on the left (Fig. 3). The urine occasionally showed pus cells and red blood cells. Further studies could not be made because the patient left against medical advice.

CASE 5 (Reg. 5866). A 40-year-old veteran had had a diagnosis of regional ileitis in 1938. Shortly thereafter, 5 feet of small bowel was resected at the University of Pennsylvania Hospital. In 1949 he spontaneously passed a renal stone (he did not know the side of origin). In February, 1951, he again developed symptoms of renal irritation, — dysuria and right-flank pain, — and was admitted to the Brooklyn Veterans Administration Hospital. The intestinal complaints of periumbilical pain and explosive diarrhea had been recurrent for the past 5 years but had not interfered with the patient's ability to work.

The admission physical examination revealed good nutrition, an indefinite tender right-lower-quadrant mass, visible abdominal peristalsis and marked clubbing of the fingers and toes. (The latter finding, the patient reported, was both congenital and familial!) The urine was completely normal.

Small-intestine x-ray films showed extensive, partially obstructive inflammatory involvement with complete loss of normal pattern of almost the entire remaining ileum. Pyelography demonstrated medial displacement of the right ureter with considerable right ureterectasia.

In April, 1951, 80 cm. of ileum and cecum and 35 cm. of ascending colon were resected. It is of interest that, in addition to the ileitis, which stopped abruptly at the cecum, an isolated cecal ulcer, 8 mm. in diameter, was found. The latter finding was the reason for the partial large-bowel resection.

Follow-up urographic studies 6 weeks after the operation were completely normal.

CASE 6 (Reg. 6116). A 35-year-old veteran gave a history of diarrhea since 1942. In that year, just prior to capture as a war prisoner at Bataan, a diagnosis of amebiasis was established and treatment with emetine, carbosone and sulfonamides was instituted, with no abatement of the complaint. During his 3 years of captivity, the diarrhea persisted; after liberation, x-ray studies revealed a diffuse ileojejunitis. Since 1946, appendectomy, ileostomy and ileotransverse colostomy with by-passing of the lesion had been carried out at different times. The diarrhea had persisted to the date of admission (2–5 loose movements per day). Examination and studies revealed good nutrition, clubbing of the fingers, a hemoglobin of 7.5 gm., a red-cell count of 3,000,000 and x-ray evidence of extensive ileitis involving the bowel proximal to the enterotransverse colostomy. Urography showed distinct right-calyx dilatation as well as dilatation of the proximal two thirds of the right ureter. The urine was persistently negative for protein and formed elements. The anemia was attributed to chronic blood loss (as evidenced by guaiac-positive stools) and the patient required transfusions from time to time. Dilatation of the right ureter has been intermittently demonstrated.

DISCUSSION

Apparently, regional ileitis must be added to the causes of ureteral obstruction, and, as has been emphasized by Harlin and Hamm,[4] the urologist must be "bowel-conscious" in cases of "atypical ureteral defects, narrowings, and displacements." By the same token, however, the gastroenterologist must extend his realm of awareness to the retroperitoneal zone in the study of regional ileitis.

The abnormal ureteral findings (dilatation and displacement) may be truly organic in nature. This is conditioned by the retroperitoneal spread of inflammation of the ileitic process so that the ureter is compromised[1] (Case 1), and with persistence of the lesion hydronephrosis may be secondary. Apparently the presenting complaints in this event may be overwhelmingly renal in nature. On the other hand, the speedily reversible nature of the ureterectasia, as demonstrated in Cases 2, 3, 5 and 6, leads

one to suspect that this finding may be reflex in nature. Substantiating this interpretation are the findings of Narath,[5] who showed similar reversible ureteral changes in such unrelated inflammatory conditions as acute cholecystitis, orchitis, appendicitis, parametritis and oöphoritis. As yet unresolved neural reflex pathways via the autonomic nervous system, stimulated by the intra-abdominal inflammation, are probably the basis of the ureteral dilatation (which may be extreme).

It is of interest that in the cases described the right ureters have generally borne the brunt of the inflammatory encirclement. However, the left side may likewise be implicated, as in Case 4, in which bilateral involvement was present.

Summary and Conclusion

Ureteral obstruction as a complication of ileitis is described. This is secondary to the retroperitoneal spread of the inflammatory process. Reversible reflex ureteral tonic changes (dilatation) are also described as occurring in regional ileitis.

References

1. Hyams, J. A., Weinberg, S. R., and Alley, J. L. Chronic ileitis with concomitant ureteritis. *Am. J. Surg.* 61:117-120, 1943.
2. Ginzburg, L., and Oppenheimer, G. D. Urological complications of regional ileitis. *J. Urol.* 59:948-952, 1948.
3. Crohn, B. B. *Regional Ileitis.* 229 pp. New York: Grune and Stratton, 1949.
4. Harlin, H. C., and Hamm, F. C. Urologic disease resulting from inflammatory conditions of bowel. *J. Urol.* (in press).
5. Narath, P. A. *Renal Pelvis and Ureter.* 429 pp. New York: Grune and Stratton, 1951. Chap. 6.
6. Hutter, K. Über das sogenannte "Psoasrandsymptom" bei Pyelographie. *Ztschr. f. Urol.* 28:721-724, 1934.

FUNGOUS DISEASE IN MAN ACQUIRED FROM CATTLE AND HORSES*

(Due to *Trichophyton faviforme*)

Otis Field Jillson, M.D.,† and William R. Buckley, M.D.‡

HANOVER, NEW HAMPSHIRE

FUNGUS acquired from cattle or horses, more popularly referred to as "barn itch," is a common disease in rural New Hampshire and Vermont. Because of its epidemiology, it is rarely observed in highly mechanized industrial cities. "Barn itch" is a disease of farmers and their families and presents characteristic clinical findings. Until the subject was reviewed in detail by Fowle and Georg[1] in 1947 and by Carney[2] in 1949, it was believed that *Trichophyton mentagrophytes* was the common pathogen of this disease. Their findings receive support from our own, in which *Trichophyton faviforme* was found to be the common causative organism. Complete clinical and mycologic data have been accumulated on 16 cases observed during the past year. These data are considered worthy of report for three reasons: they present additional mycologic findings; trauma has been found to be the usual precipitating factor; and there is marked local interest in the disease.

Clinical Picture

All patients had contact with cattle or horses or contact with persons who had acquired the disease from these animals. The disease occurs in all age groups and in both sexes. Injury is usually an important precipitating factor. The types of injury are manifold — for example, brush, thermal or chemical burns, abrasions, puncture or incised wounds, lacerations and contusions. The initial lesion occurs at the site of trauma. Diseases such as herpes simplex and contact dermatitis may also serve as a *locus minoris resistentiae*. Some specific examples

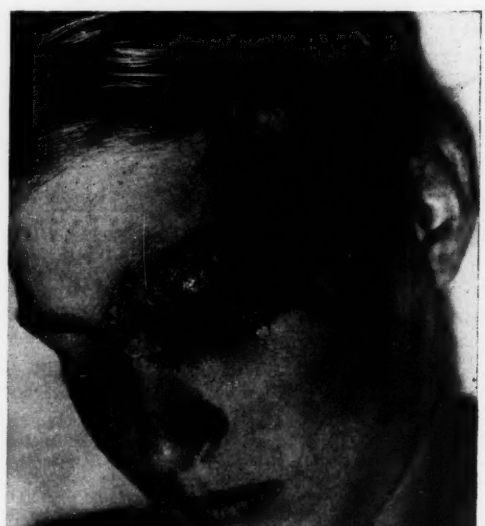


Figure 1. *Kerion.*

are as follows: wounds from shaving have precipitated the disease in 2 cases, and a puncture wound sustained while shoeing a horse in 1. Abrasion of the

*From the Hitchcock Clinic, Hanover, and the Department of Dermatology, Dartmouth Medical School.

†Instructor in dermatology and syphilology, Dartmouth Medical School; associate, Department of Dermatology and Syphilology, Hitchcock Clinic.

‡Resident in dermatology and syphilology, Hitchcock Clinic and Dartmouth Medical School.

upper eyelid sustained when the patient fell from a tree, striking a branch as he fell (Fig. 1), precipitated the disease in 1 case. Recurrent herpes simplex of the upper lip served as the initiating lesion in 2 cases; thus, contrary to popular teaching, this is not an unusual site for the occurrence of tinea barbae. Contact dermatitis following the use of a rubber "chin elevator" used in the process of giving general anesthesia precipitated the disease at this site.

After trauma, the onset of the disease is rapid. Within a few days, one or several lesions appear on the exposed surface of the body, particularly the face and arms. There are four clinical types:

Typical ringworm patches but with less tendency to central clearing (Fig. 2). These may enlarge peripherally to cover extensive areas of skin (Fig. 3).

Sharply demarcated, erythematous, edematous plaques containing grouped follicular pustules [agminate folliculitis (Fig. 4)].

Large, elevated, boggy masses covered with crusts and displaying multiple areas of draining purulent material [kerion (Fig. 1)].

Nodules with a normal overlying epidermis characterized by marked chronicity (granuloma of Majocchi).

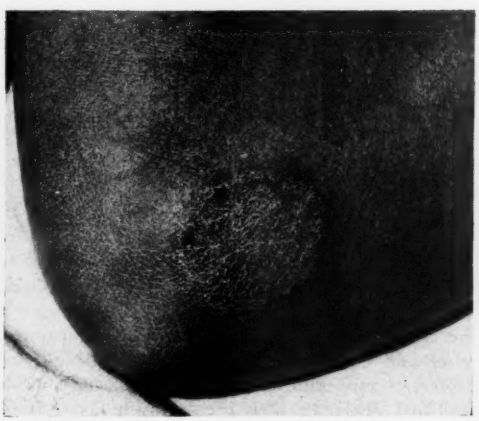


FIGURE 2. *Ringworm Type of "Barn Itch."*

Except for the ringworm type of lesion and the rare granuloma of Majocchi, the course of the disease is self-limited, with resolution in four to eight weeks. With the former types, the disease is extremely persistent unless adequately treated, or the agminate folliculitis or kerion type of the disease spontaneously appears. In its early stages, it may be accompanied by a papular dermatophytid located chiefly about the follicles and with a predilection for the trunk. This disappears spontaneously within a week. The "id" may be precipitated through the "well intentioned" use of penicillin in

FIGURE 3. *Extensive Ringworm Type of "Barn Itch."*

the treatment of the kerion. In general, despite its appearance, the disease is asymptomatic except

FIGURE 4. *Agminate Folliculitis.*

for discomfort at the site of the lesion. Hair loss and scarring are rare sequelae.

Laboratory Diagnosis

The diagnosis is established and supported by laboratory methods. Direct potassium-hydroxide (KOH) preparations can be carried out in the office and are made on the hairs, scales and purulent material from the lesions. (A drop of a 10 per cent solution of KOH is added to the suspected material on a glass slide and a coverslip applied. The slide is then gently warmed and allowed to stand for several minutes prior to microscopical examination to facilitate clearing.) A profusion of large spores is seen surrounding the hairs (large-spore ectothrix) (Fig. 5). Linear arrangement in selected specimens is readily demonstrated (Fig. 6). Occasionally

Figure 5. *Large Spores Surrounding Hair (x240).*

chains of chlamydospores may be demonstrated around the infected hairs; when this is noted, it is diagnostic of *T. faviforme*. Spores are also found in the purulent discharge. The fungus is difficult to demonstrate in the scales. This may be due to the fact that the spores, alone or associated with occasional hyphae, have been considered artefacts and previously overlooked.

Unlike other dermatophytes, *T. faviforme* requires the addition of thiamine or incubation in order to facilitate growth.[1, 2] Cultural mounts display chains of chlamydospores, some of which are enormously enlarged (Fig. 7). In addition, although no macroscopic growth is observed, we have found that hairs cultured on Sabouraud's medium at room temperature for five days and then removed show the diagnostic chlamydospores growing out from the infected hairs. In the 16 cases presented in this paper, the disease was caused by *T. faviforme*. This includes the one granuloma that is usually produced by anthropophilic fungi — for example, *Trichophyton violaceum*. *Trichophyton mentagrophytes* was found as the cause of only 1 case of "barn itch."

Histopathologic studies of early lesions are not diagnostic. They reveal moderate intercellular edema and a dense follicular inflammation consisting chiefly of polymorphonuclear leukocytes. In the case of the granuloma, monocytes and plasma cells predominated. Fungi may be demonstrated around the hairs using Schiff's stain.[3]

After the intradermal test with trichophytin 1/30 (Lederle), a persistent tuberculin type of response is obtained. Frequently associated with this reaction are malaise, headache, mild fever, lymphadenopathy and occasional joint pains. Thus, certain patients show an extremely allergic response to the trichophytin test during the course of their disease.

There is a moderate leukocytosis with eosinophilia up to 16 per cent in the peripheral venous blood.

Figure 6. *KOH Preparation of Hair, Showing Linear Arrangement of Spores (x280).*

Therapy

This disease is frequently confused with pyoderma and unnecessarily treated as such. Treatment for the kerionic lesions is directed toward symptomatic relief and consists of the application of cool wet dressings and removal of easily epilated hairs to facilitate drainage, thus promoting a faster resolution of the lesion. Here the local allergic response limits the disease. With the nonkerionic lesions and the rare granulomas, therapy is directed toward the production of folliculitis by the host with subsequent epilation. Saturated solution of potassium iodide, 5 drops thrice daily, will produce this response. Repeated injections of trichophytin have also appeared to stimulate the local allergic response. In these cases, however, the patient is advised that the lesions will appear considerably worse before spontaneous cure.

There is a suggestion that the disease produces an immunity; from personal observation and inquiry we have not found "barn itch" of the type

LIBRARY JUL 14 52 MANHATTAN KANSAS

described recurring in the same person. However, it is not definitely known whether this disease, once acquired, will protect against reinfection by this or any other fungus.

Epidemiology

Personal communication with veterinarians reveals that ringworm of horses and cattle is a common disease. The well developed lesions consist of crusty, grayish-white masses containing broken hairs. They are found on the face, neck and other parts of the body in cattle and in the saddle areas of horses (Fig. 8). The condition has been observed more

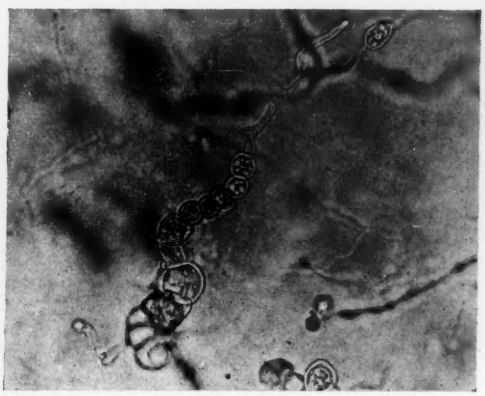


Figure 7. *Cultural Mount, Demonstrating Chains of Enlarged Chlamydospores (x315).*

frequently in calves kept in barns during the winter. The fungus survives for long periods of time in the débris around the quarters. Material from several different infected animals yielded positive cultures of *T. faviforme*. All specimens examined were heavily infected with this large-spore ectothrix.

Summary

Four clinical types of fungous disease are acquired from cattle and horses: ringworm-like patches, agminate folliculitis (grouped follicular pustules), kerion (boggy, crusted masses) and granuloma of Majocchi. Trauma is usually the precipitating factor.

Allergic manifestations include a transient papular dermatophytid and a positive tuberculin-type trichophytin skin test associated with systemic symptoms.

The common causative fungus is *Trichophyton faviforme*, a large-spore ectothrix. The diagnostic chains of enlarged chlamydospores can be demonstrated in less than one week, growing out of hairs

Figure 8. *Ringworm in Calf.*
Note crusted area on midback and bald area on neck.

that have been cultured on Sabouraud's medium at room temperature. Unless spores are carefully looked for, it is difficult to find the fungus in scales.

Owing to the marked local allergic response, the disease is usually self-limited in four to eight weeks. However, in resistant cases, iodides taken internally and repeated injections of trichophytin are of value in stimulating this reaction.

Addendum

During the months of February and March, 8 additional cases of "barn itch" have been observed. This could be partially explained on the basis of seasonal incidence, as emphasized by Davidson, Gregory and Birt.[4]

References

1. Fowle, L. P., and Georg, L. K. Suppurative ringworm contracted from cattle. *Arch. Dermat. & Syph.* **56**:780-793, 1947.
2. Carney, R. G. Inflammatory ringworm due to *Trichophyton faviform:* report of seventeen cases. *Arch. Dermat. & Syph.* **59**:209-216, 1949.
3. Kligman, A. M., Mescon, H., and DeLamater, E. D. Hotchkiss-McManus stain for histopathologic diagnosis of fungus diseases. *Am. J. Clin. Path.* **21**:86-91, 1951.
4. Davidson, A. M., Gregory, P. H., and Birt, A. R. Clinical and mycological study of suppurative ringworm. *Canad. M. A. J.* **31**: 587-591, 1934.

A COMPARISON OF THE DURATION OF ACTION OF VARIOUS LONG-ACTING ACTH PREPARATIONS IN HUMAN SUBJECTS*

WILLIAM Q. WOLFSON, M.D.,† AND STEFAN S. FAJANS, M.D.‡

ANN ARBOR, MICHIGAN

ONE criterion of the effectiveness of long-acting ACTH preparations is their duration of action. Using a simple technic, we have compared the duration of action of two types of aluminum phosphate adsorbed ACTH preparations (Adactar and Adactar Tannate) with that of certain nonadsorbed ACTH preparations. The residual eosinopenia persisting twenty-four hours after a single dose of 100 USP units of these ACTH preparations has been used as a semiquantitative method of comparing their duration of action. This type of assay may be used only in subjects who are not already receiving ACTH or cortisone. For subjects under such treatment, other assay technics are available.[1]

SUBJECTS AND METHODS

Both normal subjects and patients have been used in assay studies. The normal adults were physicians, laboratory technicians and relatives of patients with diabetes mellitus. The patients were persons with rheumatoid arthritis, eye disease, gouty arthritis or mild diabetes mellitus.

On the morning of the first day, total circulating eosinophils were enumerated by Randolph's method.[2] The subject then received a 100-unit dose of long-acting ACTH. The material was injected deeply subcutaneously insofar as possible rather than intramuscularly, and the injection site was not massaged after injection. On the morning of the second day, twenty-one to twenty-six hours after administration of the long-acting ACTH preparation, the eosinophil count was repeated.

Long-Acting ACTH Preparations

Adactar is a suspension of aluminum phosphate adsorbed ACTH (Armour) in polyvinyl pyrrolidone. Satisfactory preparations could be made in either of two ways. In the "triple-mix" method a sterile suspension of colloidal aluminum phosphate was added to sterile ACTH powder and after adsorption was complete sterile polyvinyl pyrrolidone was added. In the "single-mix" method, a sterile solution of ACTH in 60 per cent to 90 per cent propylene glycol was added to a premixed diluent ("Adactar Vehicle 40") containing suitable amounts of colloidal aluminum phosphate and polyvinyl pyrrolidone.

Adactar Tannate is identical with Adactar prepared by the "single-mix" technic, except that ACTH tannate solutions were used in its preparation. In both Adactar and Adactar Tannate, the aluminum-phosphate concentration varied from 10 to 20 mg. per cc., and the polyvinyl pyrrolidone concentration varied from 25 per cent to 30 per cent. The ACTH concentration (in terms of the USP standard) was either 20 or 40 units per cc. in all long-acting preparations studied.

Acthar-in-Oil (Adactar-0-40) is a suspension of ACTH in peanut oil and 3 per cent aluminum monostearate.§ ACTH in-Gelatin includes two types of preparations, both made from heavy gelatin and both solid at room temperature. One material (designated ANG-H) was processed from nonhydrolyzed neutralized nonantigenic gelatin (Armour). The second material (designated ADDR-H-T) was made from partly hydrolyzed neutralized nonantigenic gelatin (Duarte); in this preparation, ACTH tannate rather than ACTH was used.

RESULTS

Figure 1 summarizes results obtained in 97 individual assay studies. The 100-unit doses of long-acting ACTH used were well tolerated, and no untoward systemic effects occurred in any subject. Varying degrees of local soreness at the injection site occurred with some preparations and usually lasted from three to thirty-six hours. Figure 1 emphasizes the marked similarity in the results obtained with Adactar and Adactar Tannate. In the median subject, a single 100-unit dose of either material held the twenty-four-hour eosinophil count to below 20 per cent of the initial blood eosinophil level. In 14 of the 18 (78 per cent) subjects given Adactar Tannate and in 37 of 50 (74 per cent) receiving Adactar, the twenty-four-hour eosinophil level was less than half of the initial level.

Neither Acthar-in-oil (Adactar-0-40) nor ACTH-in-gelatin exhibited a duration of action that closely approached that of Adactar or Adactar Tannate. With Acthar-in-oil, the median twenty-four-hour eosinophil count was 49 per cent of the initial count. With ACTH-in-gelatin, the median twenty-four-hour eosinophil count was 36 per cent of the initial count. Six of 12 (50 per cent) subjects receiving Acthar-in-oil and 10 of 17 (59 per cent) subjects

*From the Rackham Arthritis Research Unit and the Metabolism Research Laboratory, Department of Internal Medicine, University of Michigan Medical School.

The Rackham Arthritis Research Unit is supported by a grant from the Horace H. Rackham School of Graduate Studies, University of Michigan, and is assisted by grants-in-aid from the National Institutes of Health, United States Public Health Service, and from the Michigan Chapter of the Arthritis and Rheumatism Foundation..

†Research associate, Rackham Arthritis Research Unit.

‡Assistant professor of internal medicine, University of Michigan Medical School; Life Insurance Medical Research Fellow.

§An abstract reporting clinical experience with Acthar-in-oil (Adactar-0-40) erroneously stated that sesame oil had been the suspension menstruum.[3] Actually, all material used was ACTH in aluminu mmonostearate and peanut oil. As yet it has not been possible to process consistently nonirritating heat-sterilized preparations using sesame oil.

given ACTH-in-gelatin showed a twenty-four-hour eosinophil count that was less than half of the initial level.

The probability that the number of subjects used in the Acthar-in-oil study was sufficiently large for assay purposes is shown by the fact that a large number of one-sided additional results would be required to make the median eosinopenia evoked by Acthar-in-oil approximate that obtained with Adactar or Adactar Tannate. For Acthar-in-oil, such a shift of median would require that each of the next 6 consecutive assay subjects have a twenty-four-hour eosinophil count below 18 per cent of the initial eosinophil count. With ACTH-in-gelatin, a similar shift of median would occur only if all of the next 9 consecutive subjects had a twenty-four-hour eosinophil count less than 18 per cent of the initial count.

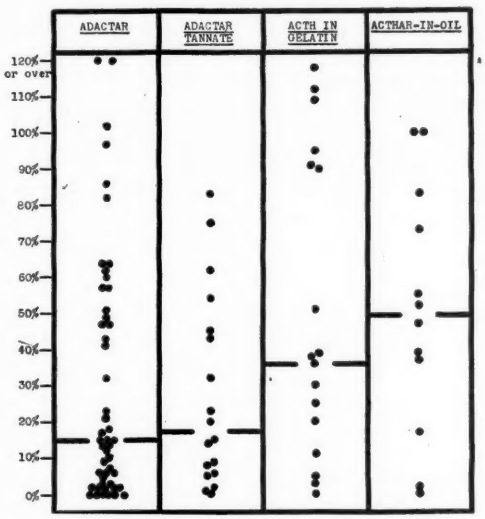


FIGURE 1. *Results Obtained with Adactar and Adactar Tannate.*

The group of subjects who received either Adactar or Adactar Tannate included 19 normal adults and 49 patients with various disorders. In both groups, the median twenty-four-hour eosinophil count was 15 per cent of the initial count. In 14 of 19 (74 per cent) normal subjects and in 37 of 49 (76 per cent) patients, the twenty-four-hour eosinophil count was less than half of the initial count. These results suggest no objection to the use of patients for this type of assay study.

Table 1 shows that the twenty-four-hour eosinopenia induced by 100-unit doses of Adactar is due solely to its ACTH content and not to any direct stressful action of the long-acting vehicle. In each of 3 subjects given 100 units of Adactar in 5 cc. of Adactar vehicle, the twenty-four-hour eosinophil count was less than 17 per cent of the initial count. Twenty-four hours after receiving 5 cc. of Adactar vehicle without ACTH, each of the same 3 subjects had an eosinophil count that was greater than 89 per cent of the initial count.

In 31 subjects the median eosinophil count twenty-four hours after a 40-unit dose of Adactar was 87 per cent of the initial count. These observations emphasize the limitations of the blood eosinophil count as a quantitative index of response to ACTH. A single eosinophil count merely indicates the response at a given instant of time. Eosinophil counts cannot be used to answer such questions as whether a single daily dose of 40 mg. of Adactar is more or less effective than four 10-mg. doses of aqueous ACTH at six-hour intervals, for there is no single time at which the counts can be taken in order to make this direct comparison. An answer to this question can be obtained by the use of semiquantitative metabolic assay procedures, as described elsewhere,[1] or by direct therapeutic studies using successive comparison technics. In 26 subjects, it was found that a single 40-unit dose of Adactar produced metabolic changes comparable to those induced by 40 units of aqueous ACTH given in divided doses over a twenty-four-hour period.[5] For the limited purposes of the present report, it should be noted that the twenty-four-hour eosinopenia after a 40-unit dose of Adactar was very much smaller than after a 100-unit dose of this material, even though many of the subjects received almost the same volume of vehicle. These observations indicate that the persistent eosinopenia after large doses of Adactar is in no way dependent on any direct action of the vehicle used. Thus, although some of the older Adactar preparations produced significant local irritation, the degree of irritation produced was

TABLE 1. *Producing No Twenty-Four-Hour Eosinopenia.*

SUBJECT	BLOOD EOSINOPHILS, HOUR 0	BLOOD EOSINOPHILS, HOUR 24	24-HOUR EOSINOPHIL COUNT
			0-HOUR EOSINOPHIL COUNT
	per cu. mm.	*per cu. mm.*	%
5 cc. of Adactar 40 vehicle containing 100 units of ACTH			
E.	272	16	6
C.	253	16	6
J.	431	75	17
Averages	*319*	*36*	*11*
5 cc. of Adactar 40 vehicle containing no ACTH			
E.	509	656	129
C.	284	253	89
J.	303	431	143
Averages	*365*	*447*	*123*

insufficient to constitute a significant stress in the subjects used for assay.

Discussion

The degree of eosinopenia that persists twenty-four hours after a single 100-unit dose of a long-acting ACTH preparation may be used as a basis for comparing the duration of action of different preparations. Single doses of this magnitude are apparently quite safe, since no untoward systemic responses were observed in 97 such studies. Either normal adults or patients may be used for this type of assay, but the subjects chosen must not be to have a duration of action and comparative metabolic potency greater than that of Acthar-in-oil. ACTH-in-gelatin has not yet been subjected to similar quantitative metabolic bioassay.

The ability of a 100-unit dose of a long-acting ACTH preparation to hold the circulating eosinophil level to less than 50 per cent of the initial level may be used as a simple, relatively crude criterion of a satisfactory twenty-four-hour ACTH preparation. According to this simple yardstick, Adactar Tannate was a satisfactory twenty-four-hour preparation in 78 per cent of 18 subjects, Adactar in 74 per cent of 50 subjects, ACTH-in-gelatin in 59 per cent of 17 subjects and Acthar-in-oil in 50 per cent of 12 subjects.

Table 2. *Additional Studies with Crude ACTH-Corticotrophins.*

Corticotrophin Preparation and Dosage	No. of Subjects	Median 24-Hour Eosinophil Count, As Per Cent of the Initial (0-Hour) Eosinophil Count
Long-acting ACTH-corticotrophins (crude corticotrophin, *USP* corticotrophin)		
100 *USP* units per dose		
Adactar, prepared from glacial acetic acid processed crude corticotrophin*	19	7
Adactar, prepared from isoelectric precipitated crude corticotrophin†	53	15
Adactar tannate, prepared from isoelectric precipitated crude corticotrophin	20	19
ACTH in heavy gelatin‡	14	31
ACTHAR-in-oil (Adactar-0-40)	22	45
ACTH in light gelatin‡	6	73
40 *USP* units per dose		
Adactar, prepared from isoelectric precipitated crude corticotrophin	31	87
ACTX-Corticotrophin (high-poteney corticotrophin; corticotrophin, purified) in heavy gelatin§		
40 *USP* units per dose	6	0
33 to 35 *USP* units per dose	17	10
20 to 25 *USP* units per dose	9	100

*Hog corticotrophin, crude (Wilson).

†Hog Acthar-A (Armour).

‡Heavy gelatin preparations cannot be given through a No. 21 needle without preliminary warming in hot water. Light gelatin preparations are easily given through No. 23 needle after being held in the hand briefly.

§H. P. Acthargel (Armour) and Purified-Corticotropin Gel. (Wilson) supplied in a 16 per cent gelatin base were brought to a gelatin concentration of 28 per cent by mixing with an equal volume of 40 per cent gelatin containing 0.5 per cent phenol.

Selection of the long-acting ACTH preparation most suitable for general clinical use does not depend solely on the various durations of action of the available materials. Such other factors as stability at room temperature, ease of administration and tendency to cause systemic hypersensitive reactions or local irritation must also be considered.

Despite an inferior duration of action, Acthar-in-oil initially appeared encouraging because of ease of administration, good room-temperature stability, fairly satisfactory local tolerance and absence of hypersensitive reactions during extensive clinical trials.[3] A later review of findings in patients who

receiving exogenous ACTH or cortisone at the time of study. At least in the case of Adactar, a preparation that tends to produce somewhat more local irritation than Acthar-in-oil or ACTH-in-gelatin, the twenty-four-hour eosinopenia does not result from any direct effect of the long-acting vehicle, since injection of the vehicle without ACTH produces no twenty-four-hour eosinopenia.

Assay data obtained by this method of comparative persistent eosinopenia indicate that Adactar and Adactar Tannate have a definite superiority in duration of action over Acthar-in-oil and ACTH-in-gelatin. This conclusion is consistent with that derived from metabolic studies reported elsewhere,[1] in which Adactar and Adactar Tannate were found

had received long-term treatment with this preparation indicated that it had an undesirable tendency to cause abscesses. Patients given 100 or more injections almost invariably developed at least one abscess. ACTH-in-gelatin enjoys a certain commercial vogue at present because of good tolerance, good stability at room temperature and simplicity of manufacture. However, when gelatin preparations are made sufficiently viscous for good prolongation of action, they are difficult to administer through moderate-sized needles, require considerable warming before being given and have an unpleasant tendency to form bubbles, which interfere with measurement of an exact dose. Adactar Tannate has no advantages over Adactar and has the disadvantage of the undesirable tannate radical. Adactar, particularly when prepared from Astwood-type crude corticotrophin (see Addendum), has a highly superior duration of action. Although early preparations caused some local irritation, this may be entirely obviated by the addition of 0.5 per cent phenol to Adactar without impairment of any of its long-acting properties. Since current Adactar is at least as well tolerated as any other preparation studied and possesses a better duration of action than all other preparations, it appears to be the most satisfactory long-acting ACTH preparation now available.

Long-acting ACTH preparations may be employed to decrease the frequency at which injections of this hormone must be given; they may also be used as an aid in decreasing the cost of ACTH treatment. Maximum economy is achieved when long-acting preparations are given every six hours as aqueous ACTH is now ordinarily administered. Use of such schedules permits a considerable saving of ACTH.[4] Alternatively, such depot preparations may be used to treat patients with a single daily injection of ACTH equal in hormone concentration to the total daily amount represented by the sum of the four doses of aqueous ACTH now ordinarily given in a twenty-four-hour period. In a few patients who need unusually large daily doses of aqueous ACTH, this result may be achieved only if two doses of long-acting material are given each day, but such patients are counterbalanced by those who are well controlled by one long-acting ACTH injection every forty-eight to seventy-two hours.[1, 3, 4]

Summary

A rapid evaluation of the duration of action of different long-acting ACTH preparations may be obtained by comparing their ability to induce a decrease in blood eosinophils that persists for twenty-four hours after a single 100-unit dose. Subjects used for these studies may be either normal adults or patients; in either case, however, they must not be receiving exogenous ACTH or cortisone at the time of the assay. In 97 such assay studies, no patient had an undesirable systemic or psychologic response to the single 100-unit dose of long-acting ACTH.

This method of analysis has been applied to four long-acting ACTH preparations. Adactar and Adactar Tannate have been found to have a duration of action clearly superior to that of either Acthar-in-oil (Adactar-0-40) or ACTH in heavy gelatin. Results with Adactar were almost identical to those obtained with Adactar Tannate. Results with ACTH-in-gelatin were slightly superior to those obtained with Acthar-in-oil. These results are consistent with previously reported results obtained in man by semi-quantitative metabolic bioassay.

Selection of a long-acting ACTH preparation for general clinical use cannot be made on the basis of duration of action alone. Such factors as temperature stability, ease of administration, tendency to cause local or systemic reactions and a number of other points should also be considered.

Acknowledgment

We are indebted to Dr. Robert E. Thompson, of the Armour Laboratories for his continued assistance and cooperation in this study. The ACTH used was supplied by the Armour Laboratories through the kindness of Dr. Harley E. Cluxton, Jr., and Dr. A. H. Holland, Jr. Dr. M. Gomez Perez, of Duarte y Compania, Havana, supplied experimental gelatin preparations. The technical assistance of Mrs. Gwendolyn Barott, Miss Wilma Barth, Miss Jane Blood, Mrs. Elizabeth Smith and Mrs. Margery Townsend is acknowledged.

Addendum

Since this manuscript was submitted for publication, two additional groups of important observations have been made. Table 2 summarizes additional studies with the long-acting crude ACTH-corticotrophins described above and with related materials. These data further confirm the superior duration of action of the Adactar-type materials. Adactar prepared from crude corticotrophin (Wilson) obtained by Astwood's glacial acetic acid process has appeared distinctly superior to Adactar prepared from crude corticotrophin obtained by the Armour isoelectric precipitation

process. As anticipated in the text, when the number of subjects who had received Acthar-in-oil was increased from 12 to 22, there was no significant change in the median twenty-four eosinopenia. The duration of action of the long-acting crude ACTH-corticotrophins has also been compared with that of the recently introduced "high-potency" purified ACTX-corticotrophins prepared most often by Astwood's process of chromatographic fractionation on oxycellulose columns. Table 2 shows that single 40-unit doses or single 33-unit to 35-unit doses of the purified ACTX-corticotrophins in heavy gelatin give a twenty-four-hour eosinopenia distinctly superior to that produced by 100-unit doses of crude ACTH-corticotrophin in heavy gelatin. Using this index, each USP unit of the "high-potency" purified ACTX-corticotrophin appears to be about as effective as 3 *USP* units of crude ACTH-corticotrophin when administered subcutaneously or intramuscularly in identical menstrua. In its ability to produce metabolic and therapeutic effects, a comparable superiority of the ACTH-corticotrophin has been demonstrated.

References

1. Wolfson, W. Q., et al. Development, evaluation, and clinical use of long-acting ACTH preparations. In *Proceedings of the Second Clinical ACTH Conference.* Edited by J. R. Mote. Vol. 2. 716 pp. Philadelphia: The Blakiston Company, 1951. Pp. 1–20.
2. Randolph, T. G. Differentiation and enumeration of eosinophils in counting chamber with glycol stain: valuable technique in appraising ACTH dosage. *J. Lab. & Clin. Med.* **34**:1696-1701, 1949.
3. Wolfson, W. Q., Thompson, R. E., Robinson, W. D., Lewis, L. and Duff, I. F. Excellently tolerated, heat-stable, long-acting ACTH preparation suitable for prolonged and ambulatory treatment. *J. Clin. Endocrinol.* **11**:800, 1951.
4. Unpublished data.
5. Wolfson, W. Q. Discussion of Forsham, P. H., Renold, A., and Lesh, J. B. Metabolic effects of small molecular ACTH: preliminary report. In *Proceedings of the Second Clinical ACTH Conference.* Edited by J. R. Mote. Vol. 1. 53 pp. Philadelphia: The Blakiston Company, 1951. Pp. 17-19.
6. Wolfson and Robinson, *Fed. Proc.* June 1951.
7. *J.A.M.A.* Raben et al. **148**:844, March 8, 1952.

CHIARI'S DISEASE — HEPATIC-VEIN THROMBOSIS*

Report of a Case

ANTHONY P. CAPUTI, M.D.,† AND THOMAS A. WARTHIN, M.D.‡

WEST ROXBURY, MASSACHUSETTS

HEPATIC-VEIN thrombosis was first described by Budd[1] in 1846 but is named for Chiari, [2] who in 1899 collected 10 cases. Since then over a hundred additional cases have been reported. The Budd-Chiari syndrome, or hepatic-vein thrombosis, may be divided into two major groups: those due to a primary endophlebitic process and others secondary to intrahepatic and extrahepatic disorders Less than 12 reported cases have been of the primary endophlebitic type. Hirsh[3] has listed many of the causative diseases leading to the secondary type, including those of thrombotic, infectious and neoplastic etiology.

The theoretical considerations of abnormalities of clot formation are probably similar to thrombotic episodes in other venous channels.

The clinical features that suggest the diagnosis of hepatic-vein thrombosis have been described as right-upper-quadrant abdominal pain due to hepatomegaly, splenomegaly, ascites, leg edema and a collateral venous pattern confined to the upper abdomen and lower thorax. This pattern is entirely independent of the collateral circulation of portal-vein thrombosis. Absent or minimal jaundice and relatively normal liver-function tests add confirmatory evidence of the disorder. Thompson[4] stated that recurrent episodes of thrombosis are the rule and that in the majority of cases the patient lives only three or four years. Occasionally survival may extend from ten to twenty-eight years. Death may be due to hepatic coma or to bleeding from an esophageal varix.

As a result of the obstruction to the outflow of hepatic blood, a centrolobular congestion may occur that is often followed by centrolobular necrosis. Central fibrosis may develop if the process continues for a long period.

In many respects, the case presented herewith is similar to the one reported by Derow and others[5] in which there was progressive thrombosis of the inferior vena cava and renal and hepatic veins. Rigdon[6] has stated that in the majority of cases of hepatic-vein thrombosis the process was secondary to inflammation of the hepatic portion of the vena cava.

Case Report

A 29-year-old man was admitted to the Veterans Administration Hospital on December 2, 1946, complaining of swelling and tenderness in the right leg. Three weeks before admission he noticed the onset of low backache with radiation down both legs. The backache ceased in 3 to 4 days, but swelling appeared in both legs, with tenderness of the calves, as well as abdominal pains, gas and constipation. After 10 days the

*From the Veterans Administration Hospital, West Roxbury.
Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements made and conclusions drawn by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

†Formerly, resident in medicine and resident in pathology, Veterans Administration Hospital, West Roxbury.

‡Clinical professor of medicine, Tufts College Medical School; chief, Medical Service, Veterans Administration Hospital, West Roxbury.

STATE COLLEGE OF AGRICULTURE AND ENGINEERING LIBRARY JUL 14 '52 MANHATTAN

left leg became normal, but he was admitted because of persistent pain and swelling of the right leg.

The past history revealed that he had been hospitalized in 1944, during military service, for a disorder characterized by fever, urticaria and anemia and that he had been given a medical discharge for schizophrenia a few weeks later.

Physical examination, which revealed a pale, well developed, well nourished man, was negative except for the liver, which was palpable and tender 2 fingerbreadths below the right costal margin, and moderate edema of the right leg. The right foot was cold and cyanotic and the right calf markedly tender, with a positive dorsiflexion sign. The temperature was 101.2°F.

Urinalysis was within normal limits. The white-cell count was 14,000, with a percentage range from 75 to 95 per cent neutrophils and eosinophils from 0 per cent on admission to 8 per cent on discharge. The hemoglobin varied from 50 to 60 gm. per 100 cc. and the red-cell count from 3,500,000 to 4,000,000. Liver tests were recorded as follows: Van den Bergh serum bilirubin 0.4 mg. per 100 cc. total, of which 0.2 mg. per 100 cc. was direct, serum cholesterol 146 mgm. per 100 cc. total and esters 146 mg. per 100 cc. The prothrombin time was prolonged to one and a half times the control. Repeated guaiac stool tests varied from + to ++++ for occult blood. The brucellergen skin test was negative. Repeated blood cultures were negative. X-ray examination of the chest was negative. Gastrointestinal series revealed changes consistent with extrinsic pressure, as if by an enlarged liver. Barium-enema examination was negative for any organic lesion of the colon or terminal ileum.

During a hospital stay of approximately 6 weeks, the patient ran a persistently spiking temperature of 101°F. daily for the initial 4 weeks, followed by an afebrile course. For the first 4 weeks generalized small to moderate lymphadenopathy was the rule; this was noted especially in both inguinal regions. The liver and spleen gradually increased in size, with the development of distended superficial veins of the anterior lower thorax and of the upper and lower abdominal wall. In the last 2 weeks of hospitalization the spleen and liver diminished in size; on discharge they were no longer palpable. Therapy consisted of adequate dicumarolization. The lymph-node enlargement diminished to within normal limits. Microscopical examination of a right cervical lymph node was negative. On discharge the patient appeared well, and the abdominal venous pattern was less prominent.

The patient was readmitted on November 10, 1948. In the 23-month interval between admissions the patient had four or five recurrences of pain and swelling of the right calf, the last occurring 1 month prior to admission, on October 11, 1948. For 2 weeks prior to admission he had been complaining of night sweats, coughing and dyspnea. The drenching night sweats preceded, by 4 days, tiredness, drowsiness, shortness of breath and a nonproductive cough. Abdominal distention was noted 2 days before entry. On the next day his physician stated that he had a "touch of pneumonia" with a temperature of 100°F. He was coughing and expectorating yellow puriform material. Weight loss was denied.

Physical examination revealed a poorly nourished, emaciated man who appeared short of breath. There was no distention of the neck veins. The abdominal venous pattern, which extended from the anterior lower thorax to the symphysis pubis, was very prominent, and there were two prominent tributaries in each flank that extended downward into the suprapubic area. There were signs of fluid at the bases of the lungs posteriorly. The heart was not enlarged; rhythm was regular. The sounds were of good quality. The aortic second sound was equal to the pulmonic. No murmurs were audible. There was mild ascites, and the abdominal wall was very tense. A mass was readily ballotted 2 fingerbreadths below the right costal margin and xiphoid. There were external hemorrhoids. Both legs appeared to be completely normal, without edema, calf tenderness or positive dorsiflexion sign.

The temperature was 101°F., the pulse 100 and the respirations 28. The blood pressure was 120/75.

Urinalysis demonstrated a pH of 5.5, a specific gravity of 1.023 and negative tests for albumin, sugar and bile; urobilinogen was positive in a concentration of 1:640; microscopical examination of the sediment revealed 4 to 6 white cells per high-power field. The white-cell count was 13,750, with 66 per cent neutrophils, 31 per cent lymphocytes, 2 per cent monocytes and 1 per cent eosinophils. The hemoglobin was 8.7 gm. per 100 c.. The red-cell count was 3,900,000. The total protein was 5.4 gm. per 100 cc. with an albumin of 1.9 gm. per 100 cc. Serum bilirubin, direct, on admission was 1.6 mg., on the 19th hospital day 1.0 mg. and on the 26th hospital day 0.6 mg. per 100 cc. The cephalin flocculation was ++ in 48 hours and the thymol turbidity was 1.6 units. The prothrombin concentration was 16 per cent of normal. The blood sugar was 119 mg. and the nonprotein nitrogen 40 mg. per 100 cc. Numerous stools were guaiac negative for occult blood and for pathogenic parasites. Several urine and blood cultures were negative. Chest fluid revealed a white-cell count of 7500 and a red-cell count of 40,000. The total protein was 4.65 gm. per 100 cc. and the specific gravity 1.015. X-ray examination of the chest showed a moderate right pleural effusion. A plain film of the abdomen revealed a diffuse haziness, consistent with ascites. Gastrointestinal series was negative; there was no evidence of esophageal varices.

The patient ran a daily spiking temperature of 101°F. for the first 5 days. It remained within the normal range until the 32nd to 34th days, when it rose to 100° or 101°F. The pulse rate was persistently over 100. On the second hospital day heparin and dicumarol therapy was started, but it was found that anticoagulant therapy could be discontinued because of persistently prolonged prothrombin times without therapy. Multiple bilateral thoracenteses, which were necessary for the relief of dyspnea, yielded serosanguineous fluid, varying in amounts from 300 to 1000 cc. On the 33rd hospital day the patient became comatose, after several days of mental cloudiness. No specific localizing neurologic signs were found, and spinal-fluid examination was negative. Jaundice was manifest on the 34th hospital day. The patient died on the 35th hospital day.

Post-mortem examination revealed a well developed, well nourished, slightly jaundiced man. There was ++ to +++ edema of both ankles. There was a right hydrothorax of 3000 cc. and ascites of 325 cc. The organs that showed important pathologic changes were the liver, lung and segments of the venous system. The femoral veins were patent, and many dilated tributaries entered them. The iliac veins were fibrous cords with no lumens; the inferior vena cava was similar to the level of the renal veins. From the level of the renal veins to above the entrance of the hepatic veins into the vena cava, the wall of the inferior vena cava was thickened, and the lumen was narrowed and irregular. The lumen was solidly filled with red-brown adherent thrombus. Above the entrance of the hepatic veins the lumen was completely obliterated, its entrance into the wall of the right auricle being represented by a puckered depression to which small gray-red fragments of clot adhered. The azygos vein was dilated to 1 cm. in diameter. The liver weighed 1320 gm. The surface was mottled red-brown, with a yellowish tinge, and on cut surface was yellow, with normal lobular markings accentuated by dark-red dots centrally. The hepatic veins contained red-brown adherent thrombi. The portal vein and its tributaries were negative, and the umbilical vein was patent. The gall bladder and bile ducts were negative. The renal veins were thick-walled, with eccentric lumens; the left was completely occluded by brown-red thrombus and the right incompletely occluded by similar thrombus. The lower lobe of the right lung was markedly atelectatic. In the artery to the lower lobe of the left lung there was an adherent gray-red laminated thrombus, but there was no infarction distally. The brain was normal. The spleen weighed 210 gm. and appeared slightly congested.

On microscopical section the inferior vena cava below the renal veins showed the oldest thrombus of very dense colla-

gen, with a peripheral ring of secondary lumens. A large vein in the prostatic capsule showed old thrombosis and recanalization. The inferior vena cava near the renal veins (Fig. 1) showed thick hypertrophic media. There was an old organ-

FIGURE 1. *Cross Section of the Inferior Vena Cava at the Level of the Renal Veins, Showing Old and Recent Thrombi.*

FIGURE 2. *Cross Section of Liver, Showing Old Hepatic-Vein Thrombosis.*

ized and recanalized thrombus and a recent thrombus that showed a small area of early organization. Several foci of lymphocytes were present in the adventitia and thrombus. The media was folded and greatly thickened. The inferior vena cava below the liver showed a large area of recent thrombus formation, which was organizing at the periphery. Above the liver this vessel revealed complete old thrombosis with slight recanalization; the scar tissue of the adventitia contained a few lymphocytes. Sections of the liver (Fig. 2 and 3) showed thromboses of two ages. A large hepatic vein contained an old recanalized peripheral thrombus and a recent central thrombus. A tributary showed old complete thrombosis and recanalization, which was contemporary with the first episode that occurred during the initial admission. Another section showed a hepatic vein with recent thrombosis and early organization and "hemorrhagic central necrosis" of the liver parenchyma. About three fourths of the liver cells were destroyed. The spleen was congested. Multiple brain sections were normal.

FIGURE 3. *Cross Section of Liver, Showing Recent Hepatic-Vein Thrombosis.*

DISCUSSION

The patient in this case exhibited the various phenomena characteristic of hepatic-vein thrombosis. The recurrent nature of the disease was emphasized. It was particularly interesting to note the joint occurrence of thrombosis of the hepatic veins and inferior vena cava during the first admission to this hospital. It may be postulated, however, that the process in the inferior vena cava antedated the hepatic-vein thrombosis, since microscopic studies revealed that the oldest thrombotic process occurred in the former. The presence of lymphocytic foci in various sections of the inferior vena cava may indicate that the process commenced as a periphlebitis and continued as an ascending process to involve other segments of this vein, the renal and hepatic veins; the thrombotic processes were then secondary. The recovery during the first admis-

sion was undoubtedly due to a combination of recanalization and incomplete thromboses of these vessels. Active thrombosis apparently occurred despite significantly low prothrombin determinations.

Evidences of liver decompensation were the prolonged prothrombin times in both admissions and a reversed albumin-globulin ratio with an elevated serum bilirubin and increased urinary urobilinogen excretion during the second admission. The reversal of the hepatomegaly and splenomegaly in the first admission was a good prognostic sign. Although it is generally believed that relatively normal liver tests support the diagnosis of hepatic-vein thrombosis, this case demonstrated that abnormal tests depend on the degree of hepatic damage. There was widespread hepatic-vein thrombosis and "hemorrhagic central necrosis" of the liver parenchyma. In addition, this damage was superimposed on a previously injured organ. The physiologic sequences of hepatic-vein obstruction are explained by Simonds and Brandes,[7] who noted hepatomegaly and increased portal-vein pressure experimentally.

Although renal-vein thromboses undoubtedly occurred during both admissions, oliguria, anuria and a rising nonprotein nitrogen were not observed.

It is believed that the repeated pleural effusions were due to a combination of lowered plasma colloid osmotic pressure and elevated venous pressure within the azygos system of veins.

The cause of death was irreversible cholemia and hepatic coma.

Summary

A case of Chiari's disease, or hepatic-vein thrombosis, is presented. The clinical signs and symptoms are correlated with the post-mortem findings.

Explanations of the various phenomena are suggested. The possibility of hepatic-vein thrombosis being secondary to an initial periphlebitis of the inferior vena cava is offered as an explanation for the origin of the disease in this case.

References

1. Budd, G. *Diseases of the Liver.* 401 pp. London, England: G. J. Palmer. 1845. P. 147.
2. Chiari, H. Über Netzbildungen im rechten Vorhofe des Herzens. *Beitr. z. path. Anat. u. z. allg. Path.* 22:1-10, 1897.
3. Hirsh, H. L., and Manchester, B. Chiari's syndrome: report of case. *New Eng. J. Med.* 235:507-511, 1946.
4. Thompson, R. B. Thrombosis of hepatic veins: Budd-Chiari syndrome. *Arch. Int. Med.* 80:602-615, 1947.
5. Derow, H. A., Schlesinger, M. J., and Savitz, H. A. Chronic progressive occlusion of inferior vena cava and renal and portal veins, with clinical picture of nephrotic syndrome: report of case with review of literature. *Arch. Int. Med.* 63:626-647, 1939.
6. Rigdon, R. H. On relation between thrombophlebitis of inferior vena cava and occlusion of hepatic veins (endophlebitis hepatica obliterans). *Bull. Johns Hopkins Hosp.* 53:162-171, 1933.
7. Simonds, J. P., and Brandes, W. C. Effect of obstruction of hepatic veins on systemic circulation. *Am. J. Physiol.* 72:320-323, 1925.

MEDICAL PROGRESS

OBJECTIVES AND LIMITATIONS OF ORTHODONTIC THERAPY

LENNARD T. SWANSON, D.M.D.*

BOSTON

IT is generally agreed that about 50 per cent of the population show some irregularity in tooth alignment. The percentage of cases actually in need of treatment is less, and the figure depends on the criteria used in determining the need. Examination of the orthodontic literature reveals disagreements on this and almost every other issue. This, of course, indicates that completely satisfactory methods have not been evolved to deal with many types of malocclusions and dentofacial abnormalities.

Orthodontia is a young specialty. Clinical training has never been available in dental schools on the undergraduate level; hence the pioneers in the field were dental practitioners who devised methods for tooth movement. The mechanical aspects were stressed, and through the years new and more effective appliances appeared. The training of many orthodontists in practice today consisted of a two-week course in appliance construction; this was the only training available. Postgraduate courses are now offered by many schools, and the curriculum shows greater emphasis on orthodontia at the undergraduate level. Thinking is being directed toward the biologic requirements and limitations rather than toward the mechanical efficiency of appliance therapy. This is, of course, as it should be.

The accepted method for evaluation of occlusion is the examination of the teeth with the jaws closed and the posterior teeth in contact. Under these conditions the upper teeth are found to encase and contact the lower teeth, and the anterior buccal cusp of the upper first molar is in line with the anterior buccal groove between the cusps of the lower first molar in a person with a normal occlusion. Sufficient arch size to accommodate the teeth without excessive irregularity or crowding is also a prerequisite.

For practical purposes normal occlusion should be defined in terms of the needs of the individual. The arrangement of the teeth must be such that the life expectancy of the masticatory apparatus is not jeopardized and the aesthetics must be acceptable

*Instructor in orthodontics, Harvard School of Dental Medicine; associate orthodontist, Children's Medical Center.

to the person. A diastema between the incisors of an adolescent female may be the focal point of personality problems, whereas another person may not be aware of his malocclusion until rejected by the armed forces.

In the light of present-day dietary habits, masticatory inefficiency is not a serious handicap in the majority of malocclusions. Youngsters losing their deciduous teeth and older persons whose dentures have been mutilated by multiple extractions rarely show signs of malnutrition attributable to inability to chew. Others with good occlusions fail to chew their food because of lazy habits.

Occlusal interferences found in certain types of malocclusions are associated with premature loss of teeth through breakdown of the periodontal structures. There are no simple or accurate methods of measuring the degree of occlusal trauma or of predicting the end result in any one case. Therefore, at present, orthodontic treatment is advocated in many cases in the hope of including potential periodontal problems. Treatment later in life when damage becomes evident is of little or no benefit.

Many physicians and dentists view the value of orthodontic therapy with skepticism. Everyone knows of patients who have worn braces throughout childhood and adolescence only to find relapse in the form of crowding and irregularity of the teeth following this lengthy and costly procedure. The question of tooth decay and damage to periodontal structures during or after treatment has also been raised with justification. It is, therefore, important to review the salient features of tooth movement and the mechanical principles of orthodontic devices.

The teeth are suspended in the alveolar bone by means of the connective-tissue fibers of the periodontal membrane. This allows the tooth a small amount of physiologic movement and, most important of all, converts the forces acting in the normal axis of the tooth to be transmitted to the bone as a pull. If a force is set up that interferes with the physiologic movement of the tooth, — such as an orthodontic appliance acting on the side of the tooth, — the tooth moves away from this force until the physiologic movement is again restored. Mobility of teeth undergoing movement is increased because reorganization and regeneration of bone do not keep pace with bone resorption. This is especially true when the tooth being moved is traumatized by cuspal interferences from teeth of the opposing jaw. Once movement is completed, however, the dense bone or lamina dura is restored and mobility is again reduced to the physiologic limits. Excessive pressures may result in impaired blood supply and necrosis at the site of pressure, decreased rate of tooth movement and permanent damage in the form of root resorption. At least one type of orthodontic appliance in use at present may produce stunting of roots. It is too early to say whether or not permanent damage leading to premature loss of these teeth will take place.

Properly constructed orthodontic appliances do not increase the caries incidence if adequate oral hygiene is practiced. Because the appliances create areas that are no longer self-cleansing by means of the tongue, lips and cheeks, extra care must be exercised to keep these areas clean. The bands are carefully adapted to the individual teeth and are cemented in place. They actually tend to protect the teeth from the local factors that promotes tooth decay.

Many types of appliances, both fixed and removable, are in use for the correction of malocclusions. In this country the fixed appliances are more commonly used. They are attached to bands cemented to the teeth and are removed by the orthodontist for adjustments to activate and direct tooth movement. The fixed appliances may be attached to only two teeth; on the other hand, all or nearly all the teeth may be banded and fixed to the orthodontic arch. The multibanding technic allows the operator very positive control and permits certain types of tooth movement not readily accomplished by other means. The simpler appliances permit the teeth to move more freely and to adjust themselves in equilibrium with each other and to the musculature around them. Both types are capable of moving teeth into abnormal positions when indiscriminately used. Both have distinct advantages, depending on the needs of the case. Unfortunately, orthodontists are prone to use one type or the other almost exclusively. Although most orthodontic appliances are designed to move teeth, inclined planes are employed for the forward repositioning of the mandible. Such therapy is effective when the mandible is functionally retruded.

A true evaluation of the occlusion involves an assay of the masticatory apparatus in function. At present, research is being directed toward a better understanding of the physiology of the muscles of mastication and the relation of the jaw structures to the skull. The statistical data are as yet incomplete and do not constitute an infallible diagnostic and prognostic yardstick. The pitfalls of making linear skull measurements from x-ray films are obvious in view of the differential three-dimensional growth patterns of the bones of the skull. Cephalometric radiography is our best tool for the clinical approach to many problems, but it must not be misdirected in an attempt to reduce the human physiognomy to a few indices applicable to the population as a whole.

One such widely used standardized x-ray assay is based on a study of 20 cases of eleven-and-one-half-year-olds with good facial patterns. Although proportions, rather than standards of linear measurements, are the objectives, at least one landmark is not stable; no allowance is made for body type or age difference. The author presented limitations,

but use has led the practitioner to adapt the method to his own needs without reservations.

An entire philosophy of treatment is based on the axial inclination of the lower incisions in relation to the lower border of the mandible.

These facts may be disturbing to the reader, but it must be remembered that application of such hypotheses will add to a better understanding of the facial complex, even though their immediate objectives may not materialize.

Dentofacial abnormalities are rarely the result of a single etiologic factor. The interaction of heredity, growth, development, function and environment leads to the many types of malocclusions seen. Although examination of the end result is usually focused on the occlusion, it is not only the teeth that are involved but the whole facial complex. This includes the alveolar bone, the maxilla and mandible, the muscles of mastication and the muscles of expression. Unfortunately the clinical methods in use today cannot separate these factors accurately.

Heredity as a cause of dentofacial abnormalities was clearly demonstrated by Stockard and Johnson[1] in their classic experiments with thoroughbred dogs. Selective breeding of dogs has produced a number of pure breeds with very distinct malocclusions and facial disharmonies. In established breeds individual characteristics are uniform to a high degree. Pure breeds such as the English bull and the Pekingese show extreme disharmonies. Others, such as the German shepherd and the basset hound, have harmoniously developed faces. In their experiments, for example, Stockard and Johnson crossed the English bull with the German shepherd and found that subsequent generations showed a variety of malocclusions. Varying degrees of the maxillary deficiency characteristic of the bulldog were noted. There is, of course, little hope of eliminating the genetic influence in human beings, but heredity does set limitations on treatment, which fact the orthodontic profession has been regrettably reluctant to accept.

The growth and development of the face extends over a long period, reaching completion in the late teens or early twenties. The face grows downward and forward away from the base of the skull. It increases in height and depth but relatively little in width. Growth and differentiation of the face do not take place at a uniform rate. Growth of the jaws proceeds rapidly until the deciduous dentition is completed; after that there is very little increase in the width of the jaws. Increase in size is mainly through growth at the posterior end of the dental arches, to accommodate the permanent molars.

During this long developmental period deciduous teeth must first erupt and then be eliminated, and each individual permanent tooth must take its place in a more or less orderly sequence in order to achieve a good adult relation. The mechanism of eruption and shedding of teeth is not known. Internal secretions have been found to have no specific effects. In endocrine disturbances such as hypothyroidism and hypopituitarism, eruption is delayed — but so are growth and development in general. There is some evidence that malocclusions are more common in cases showing advanced bone age and early eruption than in those showing retarded bone age and delayed eruption.

Abnormal function and unfavorable environmental conditions in operation during development of the occlusion cause those malocclusions that are the most amenable to orthodontic treatment. Abnormalities in the use of the oral structures are probably most often compensations for local environmental factors such as tooth interferences, thumbsucking, lip habits and so forth. Frequently teeth erupt in slightly abnormal positions, causing interferences when the jaws are brought together. Function leads to self-correction if these interferences are of minor degree. If the irregularity does not readily correct itself, a youngster may shift the mandible into a so-called "convenience bite" in which he feels more comfortable because the teeth fit together in a better relation. This may be an anterior, posterior or lateral shift; if not corrected, it tends to distort growth and may eventually lead to a permanent deformity.

Dentofacial abnormalities may be dental, osseous, muscular or any combination thereof. Malocclusions of purely dental nature include ectopic eruptions, migration of teeth due to congenital absence or extraction of teeth, supernumerary teeth and other irregularities. Although treatment may often be difficult, the prognosis is generally good.

Severe crowding of teeth indicates a discrepancy between tooth size and bony support. Since the limiting factor in tooth movement is the amount of bone available, extraction of teeth is indicated if harmony can be attained by this means. There is no valid evidence that bone growth can be stimulated by tooth movement.

Disharmonies between the maxilla and the mandible may take many forms. Either arch may be too large or too small in relation to the other. A profile that appears to have a retrusive mandible may actually have a protrusive maxilla and denture, or the upper teeth alone may be displaced forward on the maxilla. Mandibular retrusion may in turn be functional or anatomic. In a given case the genetic pattern may be good but irregularity in tooth eruption may result in a distal positioning or a functional retrusion of the mandible. If such a case is treated before the occlusal pattern is well ingrained, the prognosis is excellent. On the other hand, the genetic pattern may be one that leads to a mandible of inadequate size. Here a superimposed functional retrusion will result in less than maximum expression of the already limited growth potential of the mandible. Thus treatment here is aimed at over-

coming the functional retrusion and minimizing the anatomic discrepancy. Obviously, treatment is indicated, but improvement rather than ideal correction should be the goal.

The position of the teeth is also under the antagonistic influence of the muscle complex of the lips and cheeks and the tongue. It has been shown that in cases of muscular dystrophy, facial paralysis and congenital absence of the tongue the teeth move away from the greater force toward a new equilibrium. The role of these muscles in the commonly occurring malocclusions is not so clearly defined, however. This may or may not be a delicate balance. Compensation may take place through the teeth alone, although it is more probable that the lips and cheeks adapt themselves to some extent to the configuration of the bony framework. This problem deserves careful study.

No clinical methods are available for determining the anatomic and physiologic requirements and limitations of the individual with any degree of scientific accuracy. Therefore, treatment must often be by trial and error, tempered by clinical experience. Fortunately, the facial complex is adaptive to change; hence cases can be treated successfully despite our limited means of evaluation. Significant progress in diagnostic methods may be anticipated during the next few years.

It is not within the scope of this review to discuss every type of malocclusion.* It must be emphasized that each patient has an individual problem that is the end result of one or more causative factors. In a given case the problem is, therefore, to correct or improve the deformity thus produced. Effective treatment requires recognition of potential growth, development and natural adaptive changes, as well as the acceptance of those anatomic and physiologic limitations that have produced the malocclusion. Certain generalities, however, can be made, and are included in the hope that they will be of assistance to the general practitioner and the pediatrician. They are included not for the purpose of making definitive diagnoses but rather to suggest in a limited way the rationale of orthodontic therapy as it is applied to the developing dentition.

In the period of the primary dentition we usually consider the age group from three to five years. During this period all the deciduous teeth are erupted and are functioning. The need for orthodontic treatment at this time is limited. "Convenience bites" are common and should be treated when dental interferences produce facial asymmetries or prevent or distort facial growth.

The loss of deciduous incisors through accidents does not predispose to malocclusion; therefore space maintenance is not necessary. These incisors do not serve the purpose of keeping the space open for the permanent teeth; in many cases they are not in contact with each other. In fact, spacing between deciduous incisors is normal and desirable, indicating that space is available for the larger and wider permanent anterior teeth.

From an orthodontic point of view, the deciduous molars are of the utmost importance. Carious lesions must be repaired and every effort should be made to maintain these teeth until they are shed normally. When abscessed teeth necessitate removal, mechanical space maintenance is indicated if the space shows a tendency to close.

The gradual transition from the deciduous to the permanent dentition usually takes place between the ages of six and twelve. Othodontic observation and limited intervention are indicated to allow the innate growth potentials of the facial structures full expression. Minor irregularities are common and are usually self-correcting. However, interferences may also disrupt normal development and may lead to malocclusions that when fully established may require lengthy and complicated appliance therapy.

Parents are often concerned about crowding, rotations, spacing or overlapping of the incisors during eruption. This is understandable, since this is seen as the first stage of permanent tooth alignment. These irregularities tend to improve and often correct themselves completely. Minor crowding of the lower incisors is so common in the adult population that it can be considered normal.

Flaring of the maxillary incisors is normal prior to the eruption of the permanent canines. The roots of the four incisors and the large crowns of the permanent canines occupy the narrow confines of the premaxilla. When the canines finally erupt and fill their own positions in the arch the spacing between the incisors disappears. The roots of the incisors can then assume their normal position. Orthodontic alignment of the incisors during this period is contraindicated, since it may interfere with normal eruption of the canines.

The anterior crossbite is probably the most common problem in this age group. When an upper incisor erupts lingual to the lower incisors, its position should be corrected. As eruption continues, a dental interference of greater degree develops; thus the mandible may be shifted forward, resulting in a similar relation of other incisors. If only one central incisor, for example, erupts lingually, lateral excursion of the mandible is impossible because the teeth can meet in only one position. Since the bite is "locked," attempted lateral movement of the mandible is likely to produce damage to the periodontal structures of the teeth involved. Marked gingival recession on the labial surface of the lower incisor, especially, is common shortly after the crossbite has been established.

To allow for natural changes and adjustments, appliance therapy should be kept at a minimum.

*For a comprehensive bibliography, the reader is referred to Salzmann's textbook.

Whenever possible, simple appliances should be used, to allow a maximum of occlusal freedom.

The bulk of orthodontic treatment is now carried out after the loss of the deciduous teeth. Usually this transition takes place between the ages of ten and twelve.

Once the permanent teeth (with the exception of the third molars) are fully erupted, improvement in alignment of teeth within an arch or of the relation between the teeth of one jaw to those of the other is not likely to take place spontaneously. If a problem is suspected, an orthodontic consultation is mandatory at this time; if orthodontic treatment is indicated, it can be accomplished most easily and successfully immediately after the eruption of premolars and permanent canines. As the patient grows older, abnormal patterns become more ingrained, response to tooth movement is slower and therapeutic possibilities become more limited.

Pressure habits that may alter normal growth and function include not only thumbsucking but also finger sucking, nail biting, tongue biting and lip habits.

Thumbsucking of a noticeable degree will very definitely move teeth. The typical occlusion shows protrusion of the maxillary incisors with or without retrusions of the lower incisors. Open bites may also be produced in which the upper teeth fail to meet or overlap the lower incisors. In some cases the palate and the alveolar bone directly behind the incisors are modified. The type and degree of deformity are dependent on the position of the thumb or finger and are proportional to the time and intensity of the habit.

It is generally agreed that sucking is normal and necessary during infancy. That inadequate outlet for this need will produce abnormal sucking habits was shown in animal experiments by Levy.[3] In a controlled environment, two puppies in a litter of four were prevented from sucking while feeding. Perverted habits developed; the puppies sucked themselves, each other, bedding or any other suitable object in their surroundings. On the basis of these and similar experiments, the author concluded that the sucking needs are in excess of the activity required for nutrition. This is true, but it also suggests that this need, when associated with feeding, as it normally should be, is met in shorter time than when gratification must be gained from a perverted habit. Separation of this association may result in frustration per se, later to be applied in a broader sense to encompass all the conditions in which thumbsucking has been observed.

Why sucking may persist throughout infancy and childhood, however, is not known. It is true that thumbsucking is most likely to occur when the child is hungry, tired, bored or embarrassed. Perhaps it represents an escape to the security, warmth and comfort associated with feeding in infancy. Hellman[4] believes that the habit is an acquisition that antedates birth. It may be an infantile response to frustration and emotional tension — a response that is instinctive from birth and therefore requires no complex mental integration. As the child develops, perhaps other more complex responses to similar situations may be substituted for thumbsucking. Nail biting is common in adolescence; possibly smoking is the socially accepted equivalent response among adults. Thumbsucking occurs in breast-fed as well as bottle-fed babies. Korkhaus[5] found that thumb-, lip-, and tongue-sucking habits were more prevalent in bottle-fed babies, but this has not been substantiated by other workers. Permanent damage to the occlusion is not likely to occur if the habit is abandoned spontaneously before the eruption of the permanent incisors. The occlusion may or may not be affected if the habit persists beyond this age. Thumbsucking has been considered responsible for retrusion of the mandible. This may be true, but it must be remembered that this very common type of malocclusion may be coexistent with the habit rather than caused by it. If the upper incisors are moved far enough forward to make it inconvenient or impossible for the youngster to close the lips, he is likely to rest the lower lip behind the upper incisors. Even though the thumbsucking habit is then abandoned, the lip alone will be sufficient to maintain the protrusive position of the upper incisors.

Malocclusions that are caused by extrinsic factors respond well; once they are corrected, the alignment remains stable. Permanent correction cannot be assured, however, if the habit persists. Until the causes of thumbsucking are more clearly understood, it is a safer procedure to correct the damage that may result to the occlusion than to tamper with psychologic balance or imbalance, about which we know so little. "Habit breakers" in the form of restraining devices are contraindicated. Parents should be informed that the occlusion will not suffer if the habit is abandoned before the permanent teeth erupt. It is also important to explain that any irregularity in tooth alignment produced after the age of six years can be corrected effectively and relatively inexpensively. Time spent in reassuring anxious parents is time well spent. Too often parents feel impelled to "break" the habit despite what they are told. Nagging as a means of breaking the habit will surely increase the younster's feeling of insecurity and emotional tension; it may even turn the habit into an obsession embodying all the youngster's protests and resentments.

Treatment can be accomplished most satisfactorily when the child is old enough to co-operate. This may be at about age eight but will, of course, vary with the individual. Simple removable appliances are indicated, and although they may also prevent the habit, they are used to "straighten the teeth." Usually the child will accept them readily and gracefully with this thought in mind.

The cost of orthodontic treatment has put this health service beyond the reach of most persons. The total operating time required to treat a case, the need of custom-made appliances and the limited number of after-school hours available to the orthodontist for seeing patients are reasons given for the high cost. The need or demand for service cannot be met by the present number of orthodontists. More men are specializing in the field, but the present high birth rate has also increased the need for orthodontic care. Although preventive measures will decrease the incidence and severity of malocclusions, it is indeed unlikely that this dental ill will ever be eliminated from mankind. Improved diagnostic methods, effective appliance therapy, treatment in accordance with the needs of the case rather than with the view toward the ideal — all tend to reduce both the length of treatment and the cost. In this way orthodontia is becoming more widely available, and this trend will definitely continue. We have still far to go before we can fulfill our obligations to all those in need of treatment.

300 Lomgwood Avenue

References

1. Stockard, C. R., and Johnson, A. L. Contrasted patterns and modifications of head types and forms in pure breeds of dogs and their hybrids as results of genetic and endocrine reactions. *Am. Anat. Memoirs* **19**:149-376, 1941.
2. Salzmann, J. A. *Principles of Orthodontics.* 887 pp. Philadelphia: J. B. Lippincott Company, 1950.
3. Levy, D. M. Experiments on sucking reflex and social behavior of dogs. *Am. J. Orthopsychiat.* **4**:203-224, 1934.
4. Hellman, M. Studies of etiology of angle's class II malocclusal manifestations. *Proc. Am. Soc. Orthodontists.* 246 pp. St. Louis: C. V. Mosby Co., 1921.
5. Korkhaus, G. *Handbuch der Zahnheilkunde.* **4**:256-265, 1939.

MEDICAL INTELLIGENCE

ACUTE CALCIFIC TENDINITIS AND "FROZEN SHOULDER": THEIR TREATMENT WITH ACTH*

T. B. Quigley, M.D.,† and

Albert E. Renold, M.D.‡

BOSTON

THE action of adrenocortical hormones on the inflammatory response of tissues to irritating or damaging agents and in particular the rapid regression of localized inflammatory hyperemia, edema and exudation that follows stimulation of the adrenal cortex with ACTH indicated a therapeutic trial of the hormone in certain cases of sterile inflammation in the shoulder.

Calcific deposits in the tendons of the rotator cuff of the shoulder are common; in routine chest surveys they have been noted to occur in about 5 per cent§ of the population. The majority of these are apparently innocuous, producing neither pain nor limitation of motion, but in a few, for reasons that are not clear, the encapsulated mineral becomes the focus of a sterile inflammatory reaction. The adjacent tissues become swollen and hyperemic, the overlying subacromial bursa loses its lubricating function and the calcific deposit itself increases in size even to the point of mechanical interference with motion by impingement against the acromion and coracoacromial ligament.

The full-blown acute clinical picture is familiar. The slightest motion, active or passive, of the shoulder is accompanied by great pain; sleep, even after heavy sedation, is often impossible. Untreated, the inflammation runs its course in a week or two but may leave in its wake atrophic, contracted muscles, a shrunken joint capsule, shortened ligaments and adhesions across the subacromial bursa.

Not all patients develop the complete syndrome or go through the typical acute course. In many, unchanged pain and limitation of motion of varying degree persists for days or weeks, finally to flare up or subside. In others the onset is so insidious that it cannot be remembered, and in a few cases calcium cannot be demonstrated in the roentgenogram.

The sequelae are, of course, largely the result of disuse and could be prevented if free motion could be continued throughout the course of the disease. The early interruption of the vicious spiral of pain and immobility is the aim of all the standard methods of treatment. Heat, diathermy and x-ray accelerate the natural course of the disease and are effective in rough inverse ratio to the wavelength involved. X-ray therapy, although effective, is basically destructive to tissues and cannot be repeated indefinitely. Procaine infiltration can abolish pain and permit an immediate, sometimes spectacular resumption of motion, but the underlying inflammation remains. Often the price is paid when the effect of the anesthetic wears off and an exacerbation of symptoms occurs.

The occasional permanent relief following infiltration with procaine or other longer-acting agents probably results largely from perforation and de-

*From the Departments of Surgery, Peter Bent Brigham Hospital and Harvard Medical School.

†Assistant clinical professor in surgery, Harvard Medical School; senior associate in surgery, Peter Bent Brigham Hospital.

‡Research fellow in medicine, Harvard Medical School; assistant in medicine, Peter Bent Brigham Hospital.

§Unpublished data from the X-Ray Department of the Peter Bent Brigham Hospital.

compression of the acute calcific mass itself. This is, in fact, the basis of the popular double-needling-and-irrigation treatment, which is particularly effective when calcific material can be demonstrated to be washed through the drainage needle. Not infrequently, however, this cannot be achieved easily, and the surgeon may add the trauma of multiple large-bore needle punctures to the underlying inflammation.

Operative removal of the calcific deposit is reliable and effective, but small masses of calcium, which can at times produce major symptoms, hardly seem worth a major operative procedure, and large masses, which can reasonably be expected to produce repeated acute attacks, are best removed when quiescent.

ACTH has now been employed in 6 cases of painful calcific rotator-cuff tendinitis that have been followed for six months or more. Alleviation of pain and restoration of motion occurred promptly in 3 acute cases treated within a day or two of the onset of symptoms. In 3 other recurrent, smoldering or subsiding cases, relief of pain required days rather than hours, and restoration of motion, when it did occur, was gradual. It was expected that, as in rheumatoid arthritis, inflammation would recur after withdrawal of ACTH. In no case did this happen. In all cases the vicious spiral of pain and immobility seemed to have been interrupted.

The following case is typical of the acute group of short duration of symptoms:

P. S., a 30-year-old physician, was awakened by severe right-shoulder pain. All motions of the arm were exquisitely painful. Calcium was demonstrated in the inner cuff tendons by x-ray. Thirty mg. of ACTH was given intramuscularly every 6 hours for 4 days. In 72 hours pain had completely disappeared and the range and power of motion of the shoulders were normal. No further pain occurred during the subsequent 6 months.

The more gradual effect of ACTH in the smoldering or recurrent cases of longer duration is illustrated by the following case history:

N. W., a 54-year-old woman, had suffered dull, gnawing pain in the right shoulder for 5 weeks. External rotation was limited to 50 per cent of normal and abduction in the coronal plane to 10°. Novocain infiltration was carried out without effect. Twenty mg. of ACTH was given intravenously over an 8-hour period, with improvement. The same dosage was repeated on the 2 subsequent days with further improvement. Thirty mg. of ACTH was given intramuscularly on the 4th hospital day. Two weeks later there was no pain and the range of motion was normal.

Fortunately, very few cases run the full course and end with marked mechanical limitation of motion. These, together with "frozen shoulders" resulting from trauma and other causes, constitute a group that Codman[1] accurately characterized as "difficult to define, difficult to treat, and difficult to explain from the point of view of pathology."

All, however, share certain clinical characteristics. There is a definite checkrein to active and passive motion, particularly abduction in the coronal plane and rotation in neutral. There is little or no tenderness, and pain occurs principally as a result of straining against the contracted soft tissues. The condition, as a rule, has been static for months. The onset is often insidious or there may have been an acute inflammatory episode. The integrity of the rotator cuff can be assumed, since McLaughlin's[2] studies have shown in several hundred cases that no torn cuff has been associated with a stiff shoulder.

Without treatment, disability may be permanent. Gradual stretching of contracted adherent capsule, muscles and ligaments by physical therapy, exercises and traction is safe and effective but may require a year or more and make great demands on the patient's fortitude.

Manipulation under anesthesia is immediately rewarding but is almost invariably followed by pain of truly formidable proportions lasting for several days. Motion during the period of pain is difficult if not impossible, and by the time it has subsided adhesions may re-form, muscles and capsule again contract, and ligaments thicken to even greater density and with less range of motion than before.

Two cases falling into this group of frozen shoulders were treated by ACTH alone. Pain was temporarily alleviated, but the range of motion was not increased. The following case is typical.

E. McI., a 53-year-old woman, 1 year previously had experienced pain in the left shoulder of insidious onset with gradually increasing limitation of motion over several weeks. Calcium was demonstrable in both shoulders by x-ray. After x-ray therapy, pain and limitation of motion gradually disappeared over several months. Six weeks prior to admission the same symptoms appeared in the right shoulder. Again calcium was seen in both shoulders in the roentgenograms. On admission, abduction in the coronal plane was limited to 45°, external rotation in the neutral position was 10 per cent of normal and internal rotation was 75 per cent. Active and passive attempts at further motion reproduced the pain. Thirty mg. of ACTH was given intramuscularly every 6 hours for 4 days. Pain was greatly relieved, but motion improved little if at all. Within a month pain had returned to its original level. Four x-ray treatments were then given. During the next 6 months pain and limitation of motion gradually subsided; at the last examination the over-all motion of the shoulder was 80 per cent of normal.

The pain in this and a similar case was apparently to a considerable extent the result of moderate edema and hyperemia following attempts at active motion beyond the restriction imposed by the contracted soft tissues. This was benefited by ACTH, whereas contracted muscles, ligaments and joint capsule as such were not affected by the hormone, as might have been predicted.

In 6 cases, manipulation under anesthesia was followed by the administration of ACTH. It was hoped that effective adrenocortical stimulation would reduce or inhibit the inflammatory response to the manipulation, thus preventing pain and permitting continued mobilization, during the postoperative period. This occurred in every case. The following case was typical.

J. S., a 48-year-old man, 6 months previously sustained a laceration over the right olecranon. This became infected, and antibiotics were given for 6 weeks. During this period the shoulder was kept at rest in a sling. Thereafter, motion of the shoulder was sharply limited. On examination, ab-

duction of the humerus on the scapula in the coronal plane was limited to 40°; internal and external rotation were about 60 per cent of normal. X-ray films revealed no abnormality. Twenty mg. of ACTH was given intravenously for 24 hours. Manipulation under anesthesia was carried out with several minor and one major release of tension in abducting the arm. Intravenous ACTH was continued for 7 days (20 mg. daily). A full range of painless motion was present immediately after the manipulation and was still present six months later.

All 6 patients maintained the range of motion achieved at the time of manipulation. None exhibited pain while ACTH was being administered. In one, a thirty-seven-year-old diabetic executive, manipulation was followed by a mild ulnar neuritis confined to the sensory distribution of the nerve. This was attributed to the manipulation itself.

The dosage schedule employed was individually varied but fulfilled the following criteria: rapid establishment of high initial hormone levels, maintenance of these levels until all pain and evidence of acute inflammation had disappeared and gradual withdrawal of the hormone to avoid recurrences.

At the beginning of this study ACTH was administered intramuscularly in doses of 25 to 40 mg.* every six hours. Later, 20 mg. of the hormone dissolved in 500 cc. of a 5 per cent solution of dextrose or of saline was administered daily as an intravenous infusion over a period of eight hours. This afforded much more effective and rapid adrenocortical stimulation than intramuscular administration, and afforded a considerable saving to the patient.[3] During the period of withdrawal, however, it was found convenient to employ intramuscular administration of 10 or 20 mg. first at six-hourly, then at eight-hourly and finally at twelve-hourly intervals. The total duration of ACTH administration ranged from two to five days for acute episodes of calcific tendinitis and up to fifteen days for certain of the "frozen-shoulder" group.

When the necessity for prolonged ACTH administration (over one week) was anticipated or when the sodium retention incident to the hormonal therapy seemed particularly undesirable, as in patients with heart disease, a low-sodium diet was given during the period of active adrenocortical stimulation, and daily supplements of potassium in the form of enteric-coated tablets of potassium chloride (0.9 gm. three times daily) were administered.

Established contraindications to ACTH such as psychoses, active peptic ulcer, active tuberculosis, syphilitic or other infections, bleeding tendencies or marked congestive heart failure and hypertension[4] were carefully ruled out in every case. There is no reason to believe that cortisone would not have been as effective as ACTH in this study. However, very large initial doses of the oral preparation would be required to achieve effects equivalent to the vigorous intravenous adrenal stimulation of ACTH, and careful, slow withdrawal would be imperative.

*One mg. of the preparation used was equivalent to 1 International Unit.

It is of considerable theoretical interest that the response to ACTH in these patients is in perfect agreement with what has been postulated for the action of ACTH on tissue inflammation.[4] In the early stages of the acute inflammatory reaction to any agent, while exudation and cellular infiltration predominate, ACTH and adrenal cortical hormones effectively reduce this response. When the inflammation has progressed to the stage of permanent cellular tissue damage, with degeneration and fibrosis, little or no effect can be demonstrated. In the patients described, all stages of inflammatory response were represented and responded accordingly. It is important to understand that in the "frozen-shoulder" cases ACTH affects only the acute inflammatory response that follows mobilization; the pre-existing fibrosis, with its mechanical limitation of motion, is not affected by the hormone.

On the other hand, the response of acute calcific tendinitis to ACTH and particularly the failure to relapse after discontinuation of the hormone may contribute to the understanding of the pathogenetic process involved. If the condition is initiated by a purely mechanical or unspecific irritation around the calcific deposits, followed by a self-perpetuating spiral of pain, disuse and atrophy, as has initially been proposed, then ACTH may reasonably be expected to interrupt the spiral, resulting in permanent improvement until again an irritation occurs.

Many questions remain unanswered. Whether ACTH will have any permanent effect on acute calcific tendinitis and whether the calcium deposits will eventually disappear must await the results of long-term follow-ups. The former is uncertain, the latter unlikely.

Summary

The natural history and current methods of treatment of painful calcific tendinitis of the rotator cuff of the shoulder are reviewed.

The results of ACTH therapy in 6 cases of acute and subacute calcific tendinitis are presented. All were benefited and in none did signs or symptoms return after withdrawal of the hormone. The most dramatic response occurred when symptoms were severe and of short duration.

The problem of the "frozen shoulder" as an end result of acute calcific tendinitis and from other causes is discussed. The results of ACTH therapy in 8 cases are presented. In 2, ACTH alone was followed by temporary decrease in pain and no increase in motion. In 6, manipulation followed by ACTH resulted in immediate marked, apparently permanent improvement in motion, without pain.

References

1. Codman, E. A. *The Shoulder.* 513 pp. Boston: Thomas Todd Co., 1934. P. 216.
2. McLaughlin, H. L., and Asherman, E. G. Lesions of musculotendinous cuff of shoulder. *J. Bone & Joint Surg.* 33A:1:76-86, 1951.
3. Renold, A. E., Forsham, P. H., Maisterrena, J., and Thorn, G. W. intravenously administered ACTH: preliminary report. *New Eng. J. Med.* 244:796-798, 1951.
4. Forsham, P. H. Present status of ACTH and cortisone in therapy. *M. Clin. North America* 35:1231, 1951.

LIBRARY 14 '52 MANHATTAN KANSAS

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38261

PRESENTATION OF CASE

A fifty-seven-year-old woman entered the hospital because of upper abdominal pain and discomfort.

Three years prior to entry, as part of a routine examination, a gastrointestinal series had revealed a small "hernia pressing on the esophagus." However, she was completely asymptomatic at that time. One year before admission she first noted upper abdominal pain and discomfort occurring one hour after eating. The pain, which lasted one-half to one hour, usually radiated up over the sternum, around to the back and occasionally to the left shoulder. It was not affected by posture or precipitated by any particular type of food; some relief was obtained with milk of magnesia. At the onset these attacks were infrequent, but three months before entry they increased in frequency, became more severe and were accompanied by a sense of fullness and eructations. In addition, for the few months before entry, episodes occurred during which she felt that "solid food stopped in the lower chest"; this feeling could be relieved by drinking fluids. Her appetite had decreased somewhat, and she had lost 10 pounds in weight over the six months prior to entry.

She had had diabetes mellitus for thirty-two years and had taken insulin for twenty-nine years. She had been taking iron for anemia. There was no history of nausea or vomiting, bloody or tarry stools, or change in bowel habits.

Physical examination revealed a well nourished woman in no distress. There was a cataract in the right eye. The lungs were clear. There was a Grade II aortic systolic murmur. The abdomen was normal. There was some sclerosis of the peripheral vessels in the lower extremities and absent ankle jerks.

The temperature was 98.6°F., the pulse 76 and the respirations 18. The blood pressure was 145 systolic, 70 diastolic.

The urine had a specific gravity of 1.022, gave a + reaction for albumin, a mustard sugar reaction and a negative reaction for acetone. Examination of the blood showed a hemoglobin of 13.8 gm. per 100 cc. and a white-cell count of 9,100, with 78 per cent neutrophils. A fasting blood sugar, prothrombin time, and nonprotein nitrogen were normal, as was an electrocardiogram. A gastrointestinal series revealed that the distal esophagus was distinctly abnormal, showing a small diverticulum-like outpouching about 2 cm. above the cardia. In this vicinity there was a rather broad ring of calcification surrounding the lower esophagus (Fig. 1). Just above the esophageal outpouching the esophagus was slightly narrowed and there was minimal delay in the passage of barium through this region. The stomach, which contained a fair amount of solid food, and the duodenum were not remarkable; two hours after the meal the head of the column was in the mid-ileum.

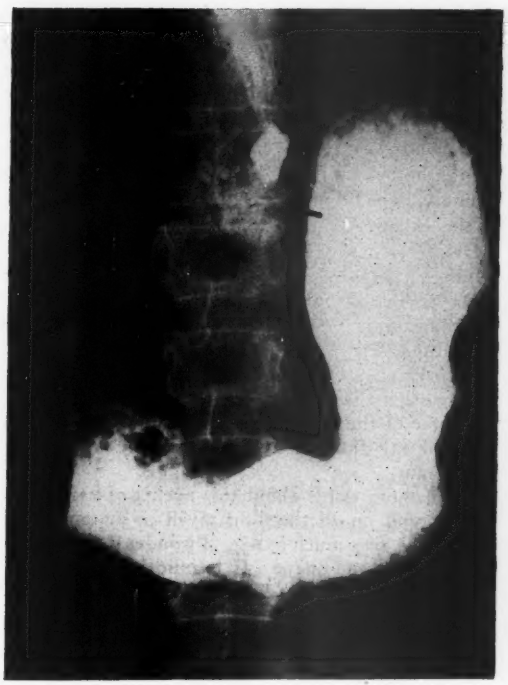


FIGURE 1. *Roentgenogram from Gastrointestinal Series. Arrows point to calcified mass.*

On the eighth day an operation was performed.

Differential Diagnosis

Dr. Richard Schatzki*: I shall reverse the usual statement made at these conferences that the x-ray films are confusing and say that the history is confusing. For that reason let me look at the x-ray films first. One can see the so-called outpouching of the esophagus. We have no right to say this actually was an outpouching of the esophagus because on none of the films can we see the esophagus in that particular area. I want to comment on the area of calcification, which is the amazing and unusual thing in this case. In this film surrounding the pocket of barium is an area of calcification apparently lobular in character (Fig. 1). It is not absolutely homogeneous, since in one area quite close to the pocket of barium there is no calcification. In the various films showing the lesion, its relation to the esophagus is very intimate. The esophagus is apparently in the center of the calcification.

Dr. Perry J. Culver: Is the lesion above or below the diaphragm?

Dr. Schatzki: On all views except the straight anteroposterior view, it appears to be below the diaphragm, but in that particular topographic area, the anteroposterior view is the one that counts. In any other than the straight anteroposterior view, the dome of the diaphragm overshadows that area. I would say the lesion is immediately above the diaphragm.

A few more words about this pocket of barium — it is present on all the films given to me and does not change very much in size. I wonder if it changed at all in size and shape. If I could be sure that it did not change at all, I should say it was a rigid cavity, most likely an area of ulceration. I cannot see the hiatus hernia described in the record as being present three years before admission.

The x-ray findings in this woman are most unusual; I have never seen anything that came even close to this appearance. What could produce anatomically such an appearance? Is it possible that the radiologist who examined this patient three years previously actually saw a hiatus hernia and that what seems to be calcification in these films is not calcification but a hernia filled by some opaque material? This could, for instance, be some material the patient had ingested, possibly barium, although it does not look like barium. A spot film in the upright position would help me. If the appearance of this mass did not change in the upright position, I would discard the possibility of a hernia filled with opaque material. Incidentally, there was no plain film of the abdomen to show whether there were any similar changes in the stomach.

What other possibilities are there? Could this have been a vascular calcification? The patient had diabetes and very likely had arteriosclerosis, although I do not see any arteriosclerosis on the films. I cannot conceive of any vascular calcification that could produce this appearance, including any possible aneurysm. The aorta is rather far from the esophagus, lying more posteriorly.

Could this have been an area of old hemorrhage close to the esophagus that had become calcified? It is conceivable, but I have never heard of such a case.

Could this have been an old abscess that had become calcified? I do not know of any mediastinal abscesses that calcify to such a degree except a tuberculous abscess. A tuberculous abscess per se, so close to the esophagus, would be unlikely — I mean an abscess outside a lymph node, arising from the spine. The lesion was not in the fascial plane of such an abscess, and I shall discard that.

Carcinomas occasionally calcify. I have never seen calcification in a primary carcinoma of the esophagus; I have seen it in the stomach and not infrequently in the colon. The appearance of the esophagus and of the calcification is highly against that diagnosis.

Could this have been a calcified tuberculous lymph node attached to the esophagus? The shape and size of the lesion are definitely consistent with that diagnosis. It is a lobulated and unusually large mass, but tuberculous lymph nodes may be large. The pocket that is seen would not be against that diagnosis. Tuberculous lymph nodes that are attached to the esophagus occasionally erode into the esophagus so that some of the barium goes into a small cavity in the lymph node. A few points are highly unusual for a tuberculous lymph node; one is the complete absence of any other evidence of tuberculosis in the films that I have. There is no plain film of the abdomen in which to look for calcified lymph nodes, but on the films of the esophagus, part of the abdomen is visible, and there is no evidence of any calcified lymph nodes. It would certainly be unusual to see one large tuberculous lymph node and none anywhere else.

Dr. Stanley M. Wyman: I believe there were some films taken before the patient came here and there was no evidence of pulmonary disease or intrathoracic disease and nothing in the abdomen to suggest calcified mesenteric lymph nodes either.

Dr. Schatzki: Could this calcified mass have been a tumor that was attached to the esophagus from the outside or arose from the wall of the esophagus below the mucosa? There are tumors in this area that may calcify, although I have never seen one that was quite like this. I have seen calcification in neurofibromas in the posterior mediastinum; they are usually not too intimately connected with the esophagus in this area. Leiomyomas in the wall of the esophagus may calcify — at least I think they may calcify. They occasionally calcify in other parts of the body. Leiomyomas of

*Clinical associate in radiology, Massachusetts General Hospital; chief radiologist, Mount Auburn Hospital, Cambridge.

the stomach have been reported as becoming calcified; those in the uterus calcify very commonly. This could have been a leiomyoma of the esophagus that had calcified and had eroded to connect with the esophagus. There are a few things that are quite unusual. First, I have never seen a calcified one; secondly, the axis of the mass is not quite in the axis of the esophagus — these tumors are ovoid in shape, and usually the long axis lies in the long axis of the esophagus. Moreover, tumors of the wall of the esophagus usually produce a characteristic appearance; they are so intimately connected with the wall of the esophagus that they cause an abrupt edge of filling on both sides of the tumor, and in a profile view the tumor can be seen projecting into the esophagus. That appearance is not recognizable on any of the films that I have at my disposal but that does not rule out such a lesion. Often the radiologist has to try to obtain this characteristic appearance, which does not offer itself; he has to flood the esophagus with barium to produce these particular features. None of these films show such flooding of the esophagus. In addition, the lesion is so close to the diaphragm, and its hiatus, that just for space reasons, its appearance may have changed.

I shall submit as my first choice, tumor of the esophageal wall, question of leiomyoma or leiomyosarcoma; and as second choice a calcified tuberculous lymph node; in either case the lesion had eroded into the esophagus.

Dr. Wyman: This lesion that Dr. Schatzki has described so very ably was really a "purple cow." We had a great deal of fun discussing it, and our line of reasoning followed his very closely. The official interpretation was in favor of calcified lymph nodes, although we had never seen such a lesion in this location. A large segment of our department did not believe this could be so and called the mass a fibroid of the esophagus, a leiomyoma, as Dr. Schatzki has concluded. We thought it might be an iceberg tumor, only a tiny amount of tumor being in the wall of the esophagus and the rest outside. We have seen it in other organs, notably the stomach.

Clinical Diagnosis

Traction diverticulum of esophagus, from calcified lymph nodes.
?Carcinoma of stomach.

Dr. Schatzki's Diagnosis

Tumor of esophageal wall, ?leiomyoma, ?leiomyosarcoma.

Anatomical Diagnoses

Leiomyoma of the esophageal wall.
Phytobezoar of stomach.

Pathological Discussion

Dr. Benjamin Castleman: This is what was carved out of the outside of the esophagus (Fig. 2). Dr. Richard H. Sweet stated in his operative note that it was adherent to the wall of the abdominal esophagus just below the diaphragm. The mass was V-shaped and surrounded the esophagus. He thought he was dealing with a mass of calcified tuberculous lymph nodes that had become adherent to the esophagus and that a traction diverticulum had developed. After removal of the mass there was a diverticulum about 2 by 1.5 cm. on the anteromedial aspect. The mass was very hard and calcified in many places. It was smooth and nodular and had

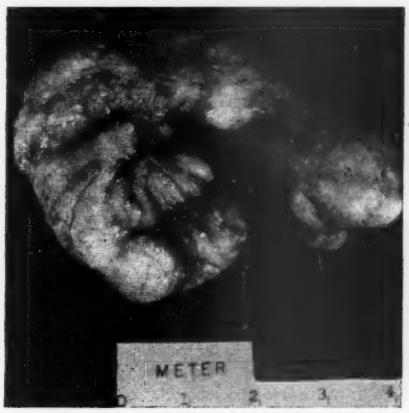


Figure 2. *Mass Removed at Operation.*

pseudopods and reminded me of a neurofibroma. Microscopically, it was a leiomyoma with a great deal of calcification in it.

Upon palpation of the stomach at operation, there was a large, soft, irregular mass, which felt at first like a polypoid tumor. A transverse incision was made across the wall of the stomach, and the mass was found to be a large accumulation of vegetable fibers amalgamated into an amorphous mass resembling tumor. This was removed, and no abnormality could be found in the stomach by palpation or inspection of the interior. In other words, this was a phytobezoar.

CASE 38262

Presentation of Case

A forty-eight-year-old man was admitted to the hospital in coma.

Eight days prior to entry, the patient had an episode of nausea and vomiting. The next day he complained of occipital headache and pain in the posterior neck muscles; from time to time he pounded his forehead and complained of some headache there. Four days before entry, he had some difficulty in walking, and his legs gave way on one occasion; there was no persistence of this complaint, and no striking weakness or dragging of either leg was noted. Two days before admission he complained of difficulty with his vision while looking at television.

During the week before entry he continued to have nausea and vomiting, and occipital and frontal headache. His legs gave way again the night before entry, but he managed to get to bed without assistance and later that evening he made a few irrational, incoherent statements. Four hours before entry, his wife awoke to find him unresponsive and breathing stertorously.

Nine months before admission he came home from work with the story of having "blacked out," but there was no further information about this episode. The blood pressure at that time was 175 systolic. The next day nausea, vomiting, and some weakness of the legs developed. After ten days he returned to work asymptomatic except for some buzzing in the ears. Six months prior to entry he became extremely irritable and often sat around apathetically not taking as much interest in current events as he had in the past. All these symptoms subsided within a month, he returned to normal, and there was no change until the present illness. His wife, however, believed that whereas he had often been difficult to get along with in the past, in the five months prior to admission he had had a definite personality change, becoming more tractable. He had had no convulsions, ataxia or slurred speech. There had been no weight loss, chronic fatigue, cough, bloody stools, abdominal discomfort or urinary difficulties.

Two years prior to entry the patient passed an insurance medical examination. There was no other past history of note.

Physical examination revealed an extremely cyanotic, deeply comatose man, with labored respirations and an obstructed airway. Because respirations had almost ceased at the time of admission an emergency tracheotomy was performed, with almost immediate restoration of normal breathing and disappearance of the cyanosis. He remained comatose but occasionally moved his arms and legs spontaneously; on several occasions nonpersisting alternating flexion-extension movements of the right leg were noted. The only response to external stimuli was withdrawal of the limbs to pinpricks. His eyes were in the midline, with no movement from side to side when his head was turned; the right pupil measured 4 mm., and the left pupil 3.5 mm., but both reacted promptly to light. Good visualization of the fundi could not be obtained initially, but eight hours later the right optic disk was thought to be elevated, with a hemorrhage, and some blurring of the left disk was noted. Corneal reflexes were absent bilaterally. There was questionable right facial weakness on supraorbital compression. The neck was not stiff. The extremities fell limply to the bed when picked up, and no extensor rigidity was noted on turning the neck. The deep tendon reflexes were all hyperactive (+++), with bilateral extensor plantar responses and bilateral ankle clonus. The palate was pulled over to the right. The lungs were clear. The heart rhythm was regular. There was a systolic murmur heard all over the precordium, but best along the left sternal border. There was a hard nonpulsatile mass, 6 by 6 cm., palpable deep in the right upper quadrant.

The temperature was 102°F., the pulse 94, and the respirations 10. The blood pressure was 160 systolic, 80 diastolic.

Lumbar puncture showed an initial spinal-fluid pressure equivalent to 540 mm. of water, with deep-yellow, cloudy fluid. The supernatant fluid showed deep xanthochromia and gave a ++ Pandy reaction. The spinal fluid contained 210 crenated red blood cells, 4 neutrophils and 10 lymphocytes per cubic millimeter. Examination of the blood showed a hemoglobin of 15.5 gm. and a white-cell count of 31,700, with 89 per cent neutrophils. The urine gave a +++ reaction for albumin and a green reaction for sugar; the sediment contained 2 to 3 red cells and 2 to 4 white cells per high-power field.

A few hours after admission the blood pressure was 210 systolic, 110 diastolic, and it persisted at this range until three hours before death. The temperature remained in the vicinity of 100°F. The deep tendon reflexes gradually disappeared, vital signs became poor, and the patient died 18 hours after admission.

Differential Diagnosis

Dr. W. H. Timberlake*: The nine-month course of this patient's illness was characterized by the episodic appearance of symptoms and their subsidence. This is not the usual course of a brain tumor but rather of vascular disease. In the last attack, beginning eight days before entry, there was nausea, vomiting, frontal and occipital headache, and neck pain. These symptoms are unusual in thrombosis or embolism except occasionally when the arteries of the brain stem are affected. However, they are a common constellation of symptoms when there is bleeding. Presumably, the headache is partly due to disruption of the vessel wall and adjacent meninges. When the headache is well localized, it may be a reliable indication of the side on which the lesion lies. Increased intracranial pressure may also be a factor in causing headache as well as the nausea and vomiting. The neck pain seems to be due to breakdown products of the blood irritating the cervical nerve roots as they pass through the subarachnoid space. This irritation, like that of meningitis, results in stiffness of the neck. The stiff neck may not be detectable for the first day or two, and it may, as in this case, be masked by coma. In the case under discussion the lumbar puncture confirmed the diagnosis of bleeding into the subarachnoid space. The initial pressure of the spinal fluid was increased, there were 210 red cells, and the fluid was a deep-yellow color although there was only a ++ Pandy — that is, the color was not due to increased protein. Crenation of red cells may occur rapidly, and the yellow color of the

*Assistant in neurology, Massachusetts General Hospital.

supernatant fluid is a more reliable way to tell that this was not just a bloody tap.

In the absence of trauma, subarachnoid bleeding may occur in several conditions. When an intracerebral hemorrhage ruptures into a ventricle the blood follows the course of the cerebrospinal-fluid circulation out through the apertures of the fourth ventricle into the subarachnoid space. Usually, such patients have arteriosclerosis and a diastolic blood pressure over 100. They quickly become comatose and remain comatose until their death a few days later. Such was not the course in this case.

Infrequently, tumors of the brain bleed into the subarachnoid space. Angiomas may bleed repeatedly over a long period, and angiomas tend to cause epileptic convulsions. In the absence of these two items in the history, the diagnosis is only a guess until confirmed by x-ray demonstration of calcification in the typical pattern, or arteriography. Gliomas and metastatic tumors have caused fatal subarachnoid hemorrhage in only 5 cases each, as confirmed by post-mortem examination here, in the past twenty-five years. I have no reason to suspect either, from the course of the neurologic symptoms. However, the mass felt in the right upper quadrant, together with the red cells in the urine, made me wonder about a renal-cell carcinoma, a tumor that may metastasize to the brain and may cause subarachnoid hemorrhage. The patient was too ill for x-ray studies, and there is insufficient evidence to establish this diagnosis.

Infected emboli in patients with subacute bacterial endocarditis may cause mycotic aneurysms, which rupture into the subarachnoid space. The history and findings give no basis for that diagnosis, nor for two other exceedingly rare causes of fatal subarachnoid hemorrhage — thrombosis of dural venous sinuses and hemophilia.

I now come to the common cause of subarachnoid hemorrhage — rupture of a congenital aneurysm. (Arteriosclerotic and syphilitic aneurysms almost never rupture.) Congenital aneurysms are probably due to a developmental defect of the muscle layer in the crotch of an arterial bifurcation. The weak area gradually bulges until the thinned wall gives way. Rarely do these aneurysms cause symptoms by direct pressure. They may cause symptoms by bursting at any age. In this hospital the age when rupture first occurred ranged from four to seventy-nine years, with a maximum number in the fifth decade, the age of this patient. The first rupture occurred at rest or during light activity in half the cases.

These aneurysms are usually located in a distal angle of the circle of Willis or at the main bifurcation of the middle cerebral artery. Almost half the aneurysms are located where the internal carotid joins the circle so rupture is likely to implicate the adjacent third nerve. Thus the common finding of ptosis, weakness of extraocular muscles supplied by the third nerve and a dilated pupil on the side of the aneurysm is not surprising. The transient blurring of vision of this patient two days before entry was not well enough described to be identified as diplopia, and in view of its late appearance and the absence of ptosis I think this symptom is more likely to have been related to the developing papilledema. Other aneurysms are difficult to localize.

The infrequent aneurysms of the basilar artery or its branches sometimes rupture against posterior cranial nerves and so may be localized. They may also interfere with circulation to the pyramids and so affect both legs. The tenth-nerve paralysis of this patient occurred late and was, I think, due to another cause, which I will mention later. Against the bilateral symmetry of leg and arm weakness I must weigh the personality changes.

Most often the aneurysm ruptures into the adjacent basal cisterns of the subarachnoid space, and no focal symptoms result until clotting closes this path and later bleeding disrupts cerebral substance, or clotting in the aneurysm thromboses the vessel with infarction. Intracerebral rupture is seen even with aneurysms of the basilar artery terminally but is most likely to occur with the aneurysms that lie in the cerebral fissures, aneurysms of the middle cerebral and of the anterior-cerebral, anterior-communicating artery bifurcations. Either of these may rupture into the frontal lobe and one can only infrequently distinguish them, as for instance when the middle cerebral aneurysms rupture into the parietal lobe. In the present case there may be another localizing hint.

I think the "black out" that the patient had nine months before entry represented the first leakage of the aneurysm. The nausea and vomiting the next day are common symptoms. One can only speculate that he probably had the usual initial severe headache. The weakness of the legs then, and again in the last attack, may indicate that I am dealing with an aneurysm of the anterior cerebral artery. The leg area of the precentral cortex is supplied by the anterior cerebral arteries. Aneurysms of the anterior cerebral arteries are not infrequently associated with an anomaly of the circle of Willis in which one anterior cerebral artery is a tiny vessel from the carotid to the anterior communicating artery, and the distal portions of both anterior cerebral arteries in effect arise from a common trunk, with the aneurysm in the crotch between them so that it might disturb bloodflow bilaterally.

The personality change six months before entry suggests disturbance in frontal-lobe function and may have represented the first intracerebral bleeding. The "irrational, incoherent statements" made the night before entry apparently were not aphasic in character and may only have been the result of the rising intracranial pressure that finally led to coma. The right facial weakness is an indication that rupture was into the left frontal lobe. Though both arms and legs moved, there appears to have been some simple repetitive activity of the

right leg, again suggesting irritation on the left. The bilateral flaccidity with increased deep reflexes should mean disturbance in the posterior part of both frontal lobes, and so there was probably some extension of the intracerebral blood into the right frontal lobe.

The absent corneal reflexes and eye movements probably reflect the depth of coma and are not localizing.

On entry the patient had an obstructed airway, which was promptly relieved by tracheotomy. Although the vocal cords are not described I suspect this man had bilateral abductor paralysis of the vocal cords due to secondary hemorrhage of the brain stem. The asymmetry of the palate suggests that the hemorrhage was primarily on the left.

Other congenital anomalies were found in 7 of the 68 cases examined post mortem here; 2 of these included polycystic kidneys. The mass in the right upper quadrant may have been a polycystic kidney.

A temperature of 101 to 102°F. and mild leukocytosis commonly accompany subarachnoid hemorrhage. About 1 patient in 20 has transient albuminuria or glycosuria. Despite the fact that this patient passed an insurance examination two years prior to admission I think the elevated blood-pressure readings were probably the more representative ones and an elevated blood pressure makes for a poorer prognosis in these patients.

My first choice of diagnoses is intracranial aneurysm of an anterior-cerebral, anterior-communicating artery bifurcation, with rupture into the left frontal lobe, with some extension into the right, and with secondary medullary hemorrhage, and ?polycystic kidneys; my second is ruptured aneurysm of the basilar artery; and my third is renal-cell carcinoma with intracerebral metastases.

DR. CHARLES S. KUBIK: There was only a small number of red cells in the spinal fluid; what do you think of that?

DR. TIMBERLAKE: I think the terminal bleeding was mainly into the cerebral hemisphere and that little of it went into the subarachnoid space. These red cells were probably residual from the event a few days before.

DR. WILLIAM H. SWEET: There was not time to do the test on this patient I am going to suggest. When the yellow color of the spinal fluid may be due to tumor or hemorrhage, the performance of a bilirubin test on the spinal fluid may aid one in solving the problem. A positive test for bilirubin would suggest that the color was indeed due to hemorrhage, as Dr. Timberlake has assumed.

DR. BENJAMIN CASTLEMAN: But if it were a tumor that was necrotic and bled, one would get the same result.

DR. SWEET: Yes; that is not quite as likely as a tumor that leaks protein into spinal fluid and gives a yellow color without bleeding.

DR. KUBIK: In those cases one would expect to find a high protein. This was not high.

CLINICAL DIAGNOSIS

Congenital aneurysm of anterior cerebral artery.

DR. TIMBERLAKE'S DIAGNOSIS

?Ruptured aneurysm of anterior cerebral or basilar artery and polycystic kidneys.

?Renal-cell carcinoma, with intracerebral metastases.

ANATOMICAL DIAGNOSIS

Renal-cell carcinoma, with multiple hemorrhagic metastases to brain.

PATHOLOGICAL DISCUSSION

DR. EDWARD P. RICHARDSON, JR.: There were many scattered hemorrhagic lesions in both cerebral hemispheres and cerebellum, with one in the medulla. From one of these lesions blood entered the left lateral ventricle. Each one of these lesions consisted of a nodule of tumor tissue completely infiltrated and surrounded by hemorrhage.

DR. CASTLEMAN: The source of the tumor was in the lower pole of the kidney, and microscopically the tumor was a classic renal-cell carcinoma with the clear cells throughout. We found no evidence of tumor anywhere else at the autopsy. There was no tumor in the renal vein and no tumor in the lungs so that the tumor must have reached the brain via the vertebral veins as has been so beautifully demonstrated by Batson.[1] At the recent meeting of the American Association of Pathologists in April an interesting paper was read in which the authors suggested another way that a tumor may metastasize to the brain. Zeidman and Buss[2] introduced a suspension of tumor cells — one of the common experimental tumors — into the venous circulation of rabbits and at the same time withdrew arterial blood from the abdominal aorta. This arterial blood was then injected intravenously into another series of animals, in 50 per cent of which tumor nodules appeared. These experiments suggest that the tumor cells would have to go through the capillaries of the lungs immediately to get into the abdominal aorta.

DR. KUBIK: The theory that the tumor cells pass through the lungs seems more likely than that cells would travel against the currents of the blood in the vertebral veins.

DR. CASTLEMAN: Batson[1] has shown that the current in the vertebral circulation is very sluggish and blood may go in either direction. He injected a dye into the dorsal vein of the penis and found the dye in the vertebral circulation, especially if he applied pressure on the abdomen to block the inferior vena cava.

Although we made a large number of sections of the lung hoping to find a few scattered tumor cells, we were unable to find any.

REFERENCES

1. Batson, O. V. Function of vertebral veins and their role in spread of metastases. *Ann. Surg.* **112**:138-149, 1940.
2. Zeidman, I., and Buss, J. M. Transpulmonary passage of tumor cell emboli. Read at the meeting of the American Association of Pathologists and Bacteriologists, New York City, April 10, 1952.

STATE COLLEGE OF AGRICULTURE & APPLIED SCIENCE KANSAS MANHATTAN JUN 14 52

The New England
Journal of Medicine

Formerly
The Boston Medical and Surgical Journal
Established 1828

Official Organ of
The Massachusetts Medical Society
and
The New Hampshire Medical Society
Owned by the Massachusetts Medical Society and Published Weekly under the Jurisdiction of the Committee on Publications

Richard M. Smith, M.D., *Chairman*
James P. O'Hare, M.D. Conrad Wesselhoeft, M.D.
Oliver Cope, M.D. Richard E. Alt, M.D.

Joseph Garland, M.D., Editor

Associate Editors
Thomas H. Lanman, M.D. Donald Munro, M.D.
Theodore H. Ingalls, M.D.

Clara D. Davies, Executive Editor
Robert O'Leary, Assistant Editor
James F. Ballard, Book Review Editor

Editorial Board
C. Guy Lane, M.D. C. Stuart Welch, M.D.
Henry R. Viets, M.D. Vernon P. Williams, M.D.
Robert M. Green, M.D. Benjamin Castleman, M.D.
Dwight O'Hara, M.D. Hugh R. Leavell, M.D.
Fletcher H. Colby, M.D. J. Englebert Dunphy, M.D.
Robert L. Goodale, M.D. Robert W. Buck, M.D.
Chester M. Jones, M.D. Herrman L. Blumgart, M.D.
Harvey R. Morrison, M.D. Frank N. Allan, M.D.
Maxwell Finland, M.D. Harvey A. Kelly, M.D.
Deering G. Smith, M.D.*

*Representing the New Hampshire Medical Society.

Subscription Terms: $8.00 per year in advance, postage paid, for the United States (medical students and first-year interns, $5.00 per year); Canada, $9.00 per year (Boston funds); foreign, $10.50 per year.

Microfilm volumes available to regular subscribers through University Microfilms, 313 N. First Street, Ann Arbor, Michigan.

Material, other than original articles, should be received not later than noon on Thursday, three weeks before date of publication.

The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts. Telephone KE 6-2094.

CUI BONO

The special recess commission that has been investigating the matter of a fourth medical school in Massachusetts, to be constructed and operated by the State, has reported favorably on the proposition. This favorable report will probably carry great weight with the Legislature, for the commission was certainly composed of the most qualified persons that could be found for such a task, and the Governor has stated that there is a desperate need within the Commonwealth for an increased number of physicians and nurses. It is, moreover, generally admitted that another dental school is needed, and a first-class dental school can hardly exist except in relation to a medical school.

The problem is, however, a complex one and requires careful scrutiny even in view of the commission's favorable report. Obviously, the only sound basis on which so costly and complicated an undertaking as the establishment of a medical school could even be considered would be the health needs of the State as they may exist some ten years from now and continue indefinitely from that time onward — for that is about the period that might be expected to elapse before the graduates of a new school could become useful adjuncts to society.

So far as the supply of physicians is concerned, Massachusetts seems at present to be about the most favorably situated state in the Union, with 1 physician per 536 of population in 1950, compared with a country-wide ratio of 1 per 749. Their distribution, classification and activities are another matter and any such discrepancies might conceivably be solved by a school dedicated to the proposition of training only or largely general practitioners pledged to remain in this state and to practice in the areas where most needed. The dangers in geographical selection have been cited by friendly critics of the proposal, and doubt has been cast on the theory that students should be recruited mainly from the rural areas. The experience of existing schools has been that it is hard enough to find good students without setting further arbitrary limitations on their selection. It is, of course, taken for granted that only a school capable of producing graduates of the highest quality will be tolerated.

Other questions need to be answered. Will a chronic-disease hospital provide all the clinical material needed for high-grade teaching? Can a faculty capable of turning out first-class physicians from the material available be assembled within a reasonable time? Will the extension and improvement of health facilities and the continued progress of preventive medicine have an effect on the number of physicians per unit of population needed to do general practice in the future?

Even in view of the very real demand for more dentists, and the desirability of having a medical school in conjunction with the needed dental school, should a new medical school be constructed with this as one of the chief arguments in its favor? Despite the fact that state help cannot be extended to a school already in operation, might not a new dental school be contrived in association with the existing medical school that does not now have one?

Perhaps the suggestion regarding a school for postgraduate training presented in these columns on June 12 should be considered, and undoubtedly other considerations will bear heavily on this important problem before a decision of unquestioned wisdom is reached. Certainly, facilities for the best possible medical service should be made available to the citizens of Massachusetts, but one cannot help recalling the editorial statement that appeared in the *Boston Herald* on May 27: "In exactly one respect a state medical school can improve on private schools — it can compel the public to make up its deficits."

THE FORSYTH DENTAL INFIRMARY FOR CHILDREN

ALMOST adjoining the Museum of Fine Arts on the Fenway in Boston is the Forsyth Dental Infirmary for Children. This institution is well known to the children of Boston who attend its clinics, but the average layman, or indeed the professional man, in Boston has a limited acquaintance with the Forsyth.

Internationally, the Forsyth needs no introduction, for it was the first institution of its kind to be erected in the world. As a philanthropic center of service, education and research, it aims not only to maintain the health of the teeth and oral structures of children, but also to conduct studies leading to the prevention of dental disease.

The history of the Infirmary goes back to 1910 when James Bennett Forsyth drew up a will leaving money for the establishment of a dental infirmary for children. Although he died before the will was signed, its provisions were carried out by his surviving brothers, John and Thomas. Little did the donors envision that a man would shortly be found to direct the destiny of this institution who had the foresight, the wisdom and the sagacity to change the current of contemporary dental thought, and to show by his research that the structure of teeth was in some way related to basic physiologic and chemical processes. This was the late Dr. Percy R. Howe, who was chief of the Research Department from the very beginning and the director of the Forsyth Dental Infirmary for Children for twenty-two years (1928–1950). His teaching and leadership promoted immeasurably the concept that dentistry must be made an integral part of the medical sciences.

The Forsyth treats hundreds of children daily, but its constant objective is to determine the factors that are responsible for the ubiquitous disease known as caries, and for the manifold deformities of the teeth commonly called malocclusions. Probably no institution in the world affords greater clinical material for study or offers better facilities for control and corrections of dental conditions in children. Students from practically every country in the world gather here each year for a better understanding of the treatment and the pathology of diseases involving the tooth structures of children. Many of these interns later hold academic positions in the United States and foreign countries.

Important investigative work is constantly being undertaken at the Forsyth, for from the beginning, Dr. Howe appreciated that dental research, to be successful, must be in partnership with other medical studies. This concept has been also the blueprint of Dr. Howard M. Marjerison, the present director, and fundamental studies are constantly in progress in the general field of child development in co-operation with the Harvard School of Public Health and the Department of Anthropology of Harvard University. While its interest is always focused upon the teeth of children, the Forsyth Dental Infirmary is directing its attention to the child as a whole — his environment, his inheritance, his diet, his intelligence, his personality and his over-all health.

Recently, at the Forsyth, orthodontic care for children has come to be regarded not only as a mechanical problem but also as one involving all aspects of health. Each prospective orthodontic patient is first examined from the point of view of his dental deformity. After this, a complete physical examination is made and the pertinent history taken by an experienced pediatrician. In this physical appraisal, great emphasis is placed upon the patient's psychologic and mental development. Next, the patient is carefully studied by an anthropologist particularly trained in the growth and development of children. Finally, a careful nutritional study is made. The patient is then discussed in conference by this group of workers, and the orthodontist decides what treatment, if any, should be instituted.

This is an illustration of the trend of dental practice at the Forsyth, where an attempt is being made to obtain a better fundamental understanding of the problems of the dentistry of children.

IMMUNIZATION IN RELATION TO POLIOMYELITIS

THE advent of poliomyelitis during the summer months, whether seasonable prevalence of the disease be high or low, brings with it a crop of answerable and unanswerable queries. In the 1940's one of the unsettled questions was the advisability of performing elective tonsillectomy during the poliomyelitis season; and gradually a rule of thumb emerged for coping with the problem — to postpone the elective operation when seasonal prevalence of paralytic and nonparalytic cases suggests that the virus is widely prevalent throughout the community. In the 1950's another question has arisen to plague physicians and public alike — whether to immunize people, particularly children, during the poliomyelitis season.

Recently representatives of the State and Territorial Health Officers Association have asked the Public Health Service to sponsor a study of the question and to issue a clarifying statement on the relation between various types of inoculation and poliomyelitis.* The conference at which this decision was made was attended by 42 investigators, epidemiologists, pediatricians, allergists and health officers who reached unanimity in their conclusions. No definite evidence exists that an increase in the number of cases of poliomyelitis has occurred as a result of injections of vaccines, drugs and other medicinal agents. There is evidence that injections for the prevention of diphtheria, whooping cough, and possibly tetanus, when given during an epidemic of poliomyelitis may on rare occasions influence localization of paralysis in the inoculated arm or leg. The Commission was in agreement that since the risk of poliomyelitis is at all times rare in infants under six months of age, it is advisable to continue immunization procedures for this age group during an epidemic of poliomyelitis. Even for older persons the risk of withholding a tetanus or diphtheria booster should be balanced against the relatively small risk of ever acquiring poliomyelitis at one particular period. Certainly there would be no reason to withhold needed antibiotic medication such as penicillin in the face of an acute infection.

Another rule of thumb appears to be emerging for coping with the new problem — to give most immunizations, and particularly elective boosters to older children, in the off-season for poliomyelitis when seasonal prevalence of paralytic and nonparalytic cases suggest that the virus is not widely prevalent.

*Editorial. Relationship between inoculation and poliomyelitis. *J.A.M.A.* 149:170, 1952.

MEDICAL SOCIETY OF LONDON

THE one hundred and seventy-second annual dinner of the Medical Society of London, according to an account in the *British Medical Journal* of March 15, was held at Claridge's on March 6. On this notable occasion, "After the loyal toasts and the customary silent toast to John Coakley Lettsom, the health of the society was proposed by Lord Radcliffe," the guest speaker of the evening. Lord Radcliffe, in thus addressing members of the medical profession from the standpoint of a member of the legal fraternity, took the occasion of expressing his interest in the "emphasis Lettsom placed upon the pleasures of dining — 'tea, punch and fine liqueurs came in their time.' "

John Coakley Lettsom, the founder of this venerable society, was one of the many London physicians of note in the eighteenth century, although, perhaps, less familiar to present generations in this country than others of his time. Born in the West Indies, the son of a Quaker cotton planter, he was forced to abandon his medical studies in England and return home on his father's death. Here, instead of finding himself a wealthy man, he discovered that his only inheritance was his father's slaves. He freed them and being then penniless practiced medicine in the islands until he had accumulated enough money to return again to his studies, which he pursued in Edinburgh, Paris and Leyden.

He then settled in London, where he became so successful, it is said, that he attended in one year 82,000 patients, customarily tiring out three pairs of horses a day. He was a disciple of Jenner, in vaccination, and established a system of dispensaries for the poor of London, in addition to founding the Society.

A somewhat ironic verse, quite out of keeping with his character, is attributed to Lettsom himself:

> When any sick to me apply,
> I physicks, bleeds and sweats 'em;
> If after that they choose to die,
> What's that to me, I. Lettsom.

It is a great point to know when to close a speech. Some persons find it equally difficult to dominate an essay with the pen.

Boston M. & S. J., *June 30, 1852*

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The summer schedule for Consultation Clinics for Crippled Children in Massachusetts follows:

Orthopedic Clinics	Date	Clinic Consultant
Gardner	July 1	Carter R. Rowe, M.D.
Haverhill	July 2	William T. Green, M.D.
Salem	July 7	Paul W. Hugenberger, M.D.
Brockton	July 10	George W. Van Gorder, M.D.
Lynn*	July 14	Daniel M. Killoran, M.D. John J. Crowley, M.D.
Springfield	July 15	Garry deN. Hough, Jr., M.D.
Pittsfield	July 16	Edward J. Coughlin, Jr., M.D.
Worcester	July 18	John W. O'Meara, M.D.
Hyannis	July 24	Paul L. Norton, M.D.
Lowell	August 1	Albert H. Brewster, M.D.
Greenfield	August 7	Charles L. Sturdevant, M.D.
Fall River	August 25	David S. Grice, M.D.

Rheumatic-Fever Clinics	Dates
North Reading	July 1, 8, 15, 22, 29
Fitchburg	July 2, 9, 16, 23, 30

Plastic Clinics	Held	Consultant
Eastern Massachusetts	Semi-monthly	Bradford Cannon, M.D.
Western Massachusetts	Monthly	Joseph M. Baker, M.D.

Physicians referring new patients to clinic should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

*This clinic serves Lynn, Lynnfield, Saugus, Nahant, Revere, Chelsea, Everett and Winthrop. Referrals should be made directly to the Lynn Hospital.

MISCELLANY

SAMUEL W. HAMILTON MEMORIAL LECTURE AND AWARD

The American Psychopathological Association has established the Samuel W. Hamilton Memorial Lecture and Award in commemoration of the unique contribution made by Dr. Hamilton to the fields of psychiatry, medicine and sociology. The recipient of the Award will be chosen each year by the Council of the American Psychopathological Association and presented with the Samuel W. Hamilton bronze medal after delivery of the Hamilton Lecture. Contributions received from members of the Association and also from members of the American Psychiatric Association who participated as sponsors will perpetuate this yearly award.

This year, at the annual meeting of the American Psychopathological Association on June 7, the first award was presented to Clarence P. Oberndorf, M.D., clinical professor of psychiatry, Columbia University College of Physicians and Surgeons, for his distinguished contribution to psychopathology. Dr. Oberndorf's lecture was entitled "Function in Psychiatry."

CORRESPONDENCE

EQUIPMENT WANTED

To the Editor: In collaboration with the Gandhi Eye Hospital, an institute of ophthalmology has been established at Muslim University, Aligarh, United Provinces, India. The Institute, which is for graduate study, is directed by Professor Alfred Leber, formerly of the University of Göttingen.

The Institute would greatly appreciate receiving material from America, especially slides. Textbooks, charts, laboratory equipment and so forth are very difficult to get in India, and surplus texts and other material even if not the latest editions, would be useful. The material can be sent direct to Dr. Zakir Husain, vice-chancellor, Muslim University, Aligarh, United Provinces, India, or if more convenient it may be sent to Arthur E. Morgan, P. O. Box 243, Yellow Springs, Ohio.

Muslim University in Aligarh is the only Moslem university in India, and it receives students from most parts of the Moslem world.

Arthur E. Morgan

Yellow Springs, Ohio

NOTICES

FIRST ARGENTINE CONGRESS OF THORACIC SURGERY

The fourth assembly of the First Argentine Congress of Thoracic Surgery, to be called "Quintas Jornadas Argentinas de Cirugía Torácica," will be held in Buenos Aires September 8-20. A group of well known American and European specialists in thoracic surgery and endoscopy will be present. All interested physicians are invited to attend.

THE CHILDREN'S MEDICAL CENTER

Every Wednesday during the summer, there will be a meeting from 12 to 1 o'clock in the auditorium of the Jimmy Fund Building, 35 Binney Street, Boston.

These meetings will be alternate medical conferences and clinicopathological conferences. There will be no 11 o'clock or 2 o'clock conference on Wednesdays during the summer months.

SOCIETY MEETINGS AND CONFERENCES

July 7-11. International Congress of Dietetics. Page 434, issue of March 13.

July 7-12. International Diabetes Federation. Page 316, issue of February 21.

July 8-11. Thirteenth British Congress of Obstetrics and Gynaecology. Page 916, issue of December 6.

July 8-14. Commonwealth and Empire Health and Tuberculosis Conference. Page 792, issue of November 15.

July 14-18. Tuberculosis Symposium. Page 800, issue of May 15.

July 14-19. International Congress of Physical Medicine. Page 998, issue of June 28.

July 24-26. Conference on Aging. Page 559, issue of April 3.

August 25-29. American Congress of Physical Medicine. Page 476, issue of March 20.

August 31-September 6. Interamerican Congress of Cardiology. Page 522, issue of March 27.

September 7-9. Combined session of the New Hampshire and Vermont State Medical Societies. Mount Washington Hotel, Bretton Woods, New Hampshire.

September 8-20. First Argentine Congress of Thoracic Surgery. Notice above.

September 24. Massachusetts Academy of General Practice. Fall meeting. Hotel Statler.

October 28-30. New England Postgraduate Assembly. Hotel Statler, Boston.

October 29. New England Obstetrical and Gynecological Society. Annual Meeting. Hotel Somerset, Boston.

November 2-7 and 10-21. Courses in Laboratory Diagnosis of Tuberculosis. Page 354, issue of February 28.

July, 1953. International Congress on Medical Librarianship. Page 316, issue of February 21.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JULY 3

Thursday, July 3

*8:30-10:00 a.m. Fracture Conference. Boston City Hospital.
*9:00-10:00 a.m. Grand Rounds. Robert Breck Brigham Hospital.
9:30 a.m. Eye-Nerve Conference. Ether Dome. Massachusetts Eye and Ear Infirmary.
*4:00-5:00 p.m. Medical Division Lecture. Mount Auburn Hospital, Cambridge.

Saturday, July 5

9:30-10:30 a.m. Electrocardiogram Interpretation. Massachusetts General Hospital.
*11:00 a.m.-12:00 m. Blood Clinic. Dr. William Dameshek. Stearns Auditorium, New England Center Hospital.

(*Notices concluded on page xv*)

AGRICULTURE AND APPLIED SCIENCE
LIBRARY
J 14 52
MANHATTAN
KANSAS

INDEX

TO

The New England Journal of Medicine

Volume 246, January 3, 1952, to June 26, 1952

PAGES ACCORDING TO WEEKLY ISSUES

Pages	No.	Date	Pages	No.	Date
1- 40	1	Jan. 3	523-560	14	April 3
41- 76	2	Jan. 10	561-596	15	April 10
77-114	3	Jan. 17	597-636	16	April 17
115-160	4	Jan. 24	637-676	17	April 24
161-204	5	Jan. 31	677-720	18	May 1
205-242	6	Feb. 7	721-760	19	May 8
243-280	7	Feb. 14	761-800	20	May 15
281-316	8	Feb. 21	801-838	21	May 22
317-354	9	Feb. 28	839-882	22	May 29
355-390	10	Mar. 6	883-918	23	June 5
391-434	11	Mar. 13	919-950	24	June 12
435-476	12	Mar. 20	951-992	25	June 19
477-522	13	Mar. 27	993-1024	26	June 26

BOOK REVIEWERS

Allan, Frank N.
Anderson, James O.
Appel, Bernard
Ballard, James F.
Bartels, Elmer C.
Benda, Clemens E.
Bland, Edward F.
Brown, Ethan A.
Brues, Austin M.
Buck, Robert W.
Carbone, Herbert A.
Castleman, Benjamin
Chute, Richard
Cogan, David C.
Colby, Fletcher H.
Daland, Ernest M.
Dameshek, William
Dearborn, Lester W.
Dodge, Carroll V.
Downing, John G.
Edwards, Edward A.
Farber, Sidney
Faulkner, James M.
Feemster, Roy F.
Fine, Jacob
Finland, Maxwell
Fitz, Reginald
Fonda, Charles P.
Friedman, Emerick
Garland, Joseph
Gigot, Albert E.
Goodale, Robert L.
Green, Robert M.
Hayden, E. Parker
Hooker, Sanford
Joslin, Elliott P.
Kazanjian, Varaztad H.
Kelemen, George
Kettle, Ronald H.
Kuhns, John G.
Lahey Clinic
Lahey, Frank H.
Lane, C. Guy
Lantz, Herman R.
Lever, Walter F.
Lombard, Herbert L.
Lowry, Franklin P.
Lurie, Moses H.
Marble, Alexander
Marshall, Samuel F.
Meigs, Joe V.
Meltzer, Philip E.
Moore, Merrill
Morrison, Hyman
Nathanson, Ira T.
Norwich State Hospital
Nowak, Stanley J. G.
O'Brien, Frederick W.
O'Hara, Dwight
O'Leary, Robert
Phaneuf, Louis E.
Pope, Alton S.
Quigley, Thomas B.
Root, Howard F.
Savitz, Harry A.
Schulz, Milford D.
Sedgwick, Cornelius E.
Shattuck, George C.
Smith, George G.
Smith, Richard M.
Sosman, Merrill C.
Spector, Benjamin
Sprague, Howard B.
Stetson, Charles G.
Stone, Moses J.
Viets, Henry R.
Waite, J. Herbert
Warren, Kenneth W.
Wesley, Elizabeth L.
Wesselhoeft, Conrad
Wheeler, Ralph E.
Wiggin, Sidney C.

KEY TO ABBREVIATIONS

bml — Boston Medical Library
c — correspondence
cr — case record
e — editorial
mdph — Massachusetts Department of Public Health
mi — medical intelligence
mms — Massachusetts Medical Society
mp — medical progress
misc — miscellany
ness — New England Surgical Society
nhms — New Hampshire Medical Society
n — notice
nn — nonclinical notes
o — obituary
*original article

SUBJECT INDEX

A

ABDOMEN. Surgery [Welch] 967 – mp
ACTH [Downing] 56, 94 – mp
[Ingraham & others] 568*
[Monto & others] 893*
[Quigley & Renold] 1012 – mi
[Sass] 583 – mi
[Wolfson & Fajans] 1000*
ADAPTATION. Human 516 – e
ADENOMA. Parathyroid [Albright] 460 – cr
ADENOMATOSIS. Pulmonary [Badger] 262 – cr
ADOPTION 835 – e
ADRENOCORTICAL insufficiency [Nussbaum & others] 289*
AGED. Food for 591 – e
ALCOHOL. Antabuse reaction [Ayres] 276 – mdph
Inhalation [Gootnick] 277 – c
[Luisada] 38 – c
AMERICAN ACADEMY OF DENTAL MEDICINE, May 29–31, 476 – n
AMERICAN ACADEMY OF GENERAL PRACTICE, Mar. 24-27, 354 – n
AMERICAN ACADEMY OF PEDIATRICS, May 22, 522 – n
AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS, June 19-21, 434 – n
AMERICAN ASSOCIATION OF HISTORY OF MEDICINE, 242 – n
AMERICAN COLLEGE OF ALLERGISTS, Apr. 7-9, 390 – n
AMERICAN COLLEGE OF CARDIOLOGY, June 6 and 7, 760 – n
AMERICAN COLLEGE OF CHEST PHYSICIANS, Mar. 24-28, 160; June 5-8, 280 – n
AMERICAN COLLEGE HEALTH ASSOCIATION, May 1-3, 634 – n
AMERICAN COLLEGE OF PHYSICIANS, Apr. 21-25, 522 – n
AMERICAN COLLEGE OF SURGEONS, Feb. 11-12, 160; May 15-17, 596 – n
[Saunders] 203 – c
AMERICAN CONGRESS OF PHYSICAL MEDICINE, Aug. 25-29, 476 – n
AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY, May 10 and 11, 390 – n
AMERICAN HEART ASSOCIATION. Campaign 313 – e
AMERICAN MEDICAL ASSOCIATION. Gavel 714 – e
AMERICAN NEUROLOGICAL ASSOCIATION, May 8-10, 559 – n
AMERICAN PSYCHIATRIC ASSOCIATION, Feb. 28-29, 280 – n
AMERICAN PSYCHOSOMATIC SOCIETY, Mar. 29 and 30, 390 – n
AMERICAN RED CROSS 352 – e
AMERICAN Way of Life 110 – e
AMYLOIDOSIS [Baker] 146 – cr
[Craige] 302 – cr
ANCIENT sacrifice (Kingship. Britain) 593 – e
(DAVID) ANDERSON-BERRY prize (1953) 635 – n
ANEMIA. Sickle cell [Sass] 583 – mi
ANESTHESIA. Intradermal labor [Abrams] 203 – c
ANEURYSM. Ruptured [Wheeler] 151 – cr
ANNOUNCEMENTS
Fenn, George K. 159
Hoyt, Lyman H. 676
Kaplan, Isadore 595
McHugh, James V. 114
McKeogh, Robert P. 353
Ridder, William P. 950
Sullivan, Charles L. 159
ANTABUSE [Ayres] 276 – mdph
ANTIBIOTICS 240 – e
[Kass & others] 167*
[MacCready] 518 – mdph
[Ravreby & others] 883*
Mental complications [Clark & others] 205*
Treatment [Stillman & Ganong] 293*
AORTA. Abdominal. Embolus [Adams] 982 – cr
Abdominal. Ruptured [Wheeler] 151 – cr
Aneurysm. Treatment [Linton & Hardy] 847 – ness
APPENDICITIS [Bartlett] 627 – cr
ARCHEOLOGIC triumph [Springer] 799 – c
ARGENTINE Congress of Thoracic Surgery, Sept. 8-20, 1024 – n
ARROW wounds [Lundy] 444*
ART 112 – e
ARTERIES. Obstruction [Dunlop] 219 – ness
ARTERIOSCLEROSIS. Coronary [Burnett & Gundersen] 449*
ARTHRITIS 390 – n
And rheumatism 914 – e
ASBESTOSIS [Arnott] 867 – cr
ASTHMA [Rackemann & Edwards] 816, 858 – mp
Infectious [Mueller & Flake] 924*
ATHLETICS. Trauma [Thorndike] 335 – mp
ATOMIC accidents 799 – e
Radiation 390 – nn
AUREOMYCIN [Rutenburg & others] 52*
Administration [Siegel & others] 447*
AUTOMOBILE. Accidents 74 – e
AYCOCK, WILLIAM LLOYD 158 – o

B

(THOMAS P.) BEATTY. (Suspension of License) [Cochrane] 634 – c
BENZEDREX inhaler [Burnett & Gundersen] 449*
BETH ISRAEL HOSPITAL. Medical Service, Jan. 30, 160 – n
Refresher course 800 – n
(ROBERT B.) BIGELOW. (Suspension of License) [Cochrane] 634 – c
BILIARY obstruction [Mellinkoff & others] 729*
Tract surgery [Hight & Lingley] 761 – ness
BLOOD BANKS. Licensing 836 – mdph
Coagulation 240 – e
BLUE CROSS 948 – e
BONE lesions. Needle biopsy [Rix & Brooks] 373 – mi – ness
BOOKPLATES. Medical 558 – e
BOOK REVIEWS
Bases of Human Behavior [Saul] 757
Bonnin, J. G. 159
Bortz, E. L. 916
Campbell, H. J. 242
Cash, J. E. 915
Cobb, S. 675
Conquest of Malaria [Jaramillo-Arango] 881
Devereux, G. 278
Diabetes Control [Bortz] 916
Diseases of the Heart and Circulation [Wood] 881
Dollar, J. 758
Emotions and Clinical Medicine [Cobb] 675
Functional Anatomy of Limbs and Back [Hollinshead] 75
Gallagher, J. R. 915
Goldberger, E. 916
Heart Disease [Goldberger] 916
Hollinshead, W. H. 75
Hunter, F. T. 758
Injuries to Ankle [Bonnin] 159
Jaramillo-Arango, J. 881
Kleinberg, S. 278
Liberman, J. B. 242
Lockwood, D. P. 675
Miller, N. E. 758
Personality and Psychotherapy [Dollar & Miller] 758
Physicians Federal Income Tax Guide [Campbell & Liberman] 242
Psychoanalysis, Man, and Society [Schilder] 757
Quantitation of Mixtures of Hemoglobin Derivatives by Photoelectric Spectrophotometry [Hunter] 758
Reality and Dream: Psychotherapy of a Plains Indian [Devereux] 278
Saul, L. J. 757
Schilder, P. 757
Scoliosis: Pathology, etiology and treatment [Kleinberg] 278
Terminal Care for Cancer Patients 39
Textbook of Medical Conditions for Physiotherapists [Cash] 915
Ugo Benzi: Medieval philosopher and physician, 1376–1429 [Lockwood] 675
Understanding Your Son's Adolescence [Gallagher] 915
United States Public Health Service, 1789–1950 [Williams] 916
Williams, R. C. 916
Wood, P. 881
BOSTON CITY HOSPITAL. Alumni Association, Apr. 26, 476 – n
Fracture Service, Feb. 6, 114 – n
House Officers' Association, Feb. 5-26, 160; Mar. 18-Apr. 15, 476; Apr. 22-29, 559; May 6–June 3, 634; June 5, 760 – n

Boston Dispensary Proctologic Session, May 10, 433 – n
Boston Floating Hospital, Apr. 7, 521 – n
Boston Gastroenterological Society, Mar. 26, 354 – n
Boston Guild for Hard of Hearing 632 – e
Boston Lying-in Hospital. Postgraduate Course 313 – e
In Obstetrics and Pediatrics, Apr. 17-19, 315, 433 – n
Boston Medical Library, May 19, 715 – n
(Conan) Doyle 472
Medicine. Jewish 472
Nobel prizes 276
Plague. History 517
(Benjamin) Rush 314
Science Librarians 202
(Miguel) Servet 517
Boston Society of Biologists, Feb. 13, 204; Apr. 2, 521 – n
Boston University School of Medicine Alumni Association, May 3, 560 – n
Brass. Dermatitis [Morris] 366*
Breast cancer [Lewison & Chambers] 1*
Prognosis [McManus & Sommers] 890*
Brill's Disease 386 – e
Britain 593 – e
Bronchiectasis [Lerman] 230 – cr
Brucellosis [Sharp & others] 485*
Buffalo Surgical Society 315 – nn
(Frank E.) Bunts Educational Institute, Apr. 3-5, 434 – n
Butler Hospital 672 – e

C

Cadavers. X-Ray identification 73 – e
Campaigns. Fund raising 470 – e
Canada. Diseases 755 – e
Cancer. Campaign 516 – e
Epidemiology 515 – e
Hormonal treatment [Nathanson & Kelley] 135, 180 – mp
[Lewison & Chambers] 1*
Prevention [Wynder] 492, 538, 573 – mp
Seminar, Apr. 21-25, 114 – n
Surgery [Ulfelder & Meigs] 243 – ness
Carcinoma [Berg] 505 – cr
[Colcock] 391 – ness
[Reeves] 652 – mp
Renal cell [Timberlake] 1017 – cr
Metastasis [Starr & Miller] 250*
Chauvinism 199 – e
Chiari's disease [Caputi & Warthin] 1004*
Children's Cancer Research Foundation, May 13 and 20, 676 – n
Children's Hospital, Apr. 17-19, 315 – n
Postgraduate Course 313 – e
Obstetrics and Pediatrics, Boston Lying-in Hospital, Apr. 17-19, 351, 433 – n
Children's Medical Center, Feb. 27, 280; Apr. 29, 635; 1024 – n
Chloramphenicol [Workman & others] 962*
Cholangiograms [Hight & Lingley] 761 – ness
Cholesterol [Thannhauser] 695 – mp
(Henry A.) Christian 310 – e
Memorial Library [Schnitker] 315 – c
(Edward D.) Churchill 315 – nn
Cirrhosis [Adams] 102 – cr
Hepatic [Jacobson] 749 – cr
Civil Defense [Cauley] 594 – c
Administration. Medical Directors 760 – n
Massachusetts 159
Colitis. Ulcerative [Ellis] 664 – cr
[Patterson & Eytinge] 691*
College of Medical Evangelists, Mar. 2-4, 280 – n
Coma. Diabetic [Haigh & Perry] 113 – c
Conference on Aging, July 24-26, 559 – n
Corti 428 – e
Cortisone [Downing] 56, 94 – mp
[Ingraham & others] 568*
[Sass] 583 – mi
[Workman & others] 962*
Craniopharyngiomas [Ingraham & others] 568*
Crystalloid-colloid relations 633 – e
[Butt & Hauser] 604*
Cutter Lecture. Obstetrics [Baird] 561*
Cyst. Dermoid [Burgin] 424 – cr
Cystitis emphysematosa [Milner & others] 902 – mi

D

Deaths
Aycock, William Lloyd 158 – o
Bachmann, Rudolph F. 673
Barrett, Edward W. 915
Barron, Elmer W. 471
Blanchard, William H. 112
Brickett, Beatrice H. 37
Burns, Thomas F. 799
Calitri, Constant 313
Casey, John F. 471
Clarke, Harry C. 471
Fishman, Maurice 314
Flynn, George C. 880
Flynn, William A. 799
Gallupe, Harold Quimby 991 – o
Garrick, Nathan H. 157
Gear, Patrick E. 314
Gillis, John E. 37
Gingras, Albert F. 593
Gray, George H. 471
Holbrook, Charles A. 799
Lancaster, Walter B. 37
Lee, Joshua M. 471
Look, Percy J. 37
Lynch, William F. 880
Mallory, Tracy Burr 273 – o
Mangurian, Armen S. 353
Metcalf, Carleton R. 353
Miles, George A. 112
Molotchick, Maxwell B. 314
Monahan, John A. 471
Mongan, Charles E. 715
O'Day, George F. 314
Parker, Willard S. 471
Perkins, Harry B. 112
Phelps, O. Draper 112
Phippen, Hardy 157
Pitcher, Hervey B. 799
Pratt, Ezekiel 314
Reilly, Thomas E. 471
Rondeau, Leo G. 593
Ryder, Delano R. 37
Smithwick, Marsena P. 673
Stansfield, Clarence W. 915
White, Arthur W. 353
Winslow, Benjamin S. 715
Wood, Nathaniel K. 314
Woodman, Ernest L. 314

(George P.) Denny 595 – nn
Depo-Heparin [Holyoke & Wheelwright] 15*
Dermatitis. Industrial [Morris] 366*
Therapeutic 111 – e
[Lane] 77*
Dermatomyositis [Lever] 585 – cr
Dever, Governor 111 – e
Diabetes Fair [Blotner & others] 520 – c
Mellitus and coronary thrombosis [Robinson] 332*
New journal 387 – e
Tuberculous [Ferrara] 55*
Digitalis poisoning [Cohen] 225, 254 – mp
Diphtheria 518 – mdph
Disabled. Aid 470 – e
District Societies. Publications 631 – e
Diverticula. Duodenal [Cattell & Mudge] 317 – ness
Doctors Afield
Dr. Archagathos: Refugee Physician and Roman Consul [Buck] 866 – mi
(Conan) Doyle 472 – bml
Drugs. Antihypertension 947 – e
Duodenal ulcer [Adams] 872 – cr
Dupuytren's contracture [Tanzer] 807 – ness
Dyspnea [Palfrey] 826 – mi
Dysuria. Tripelennamine [Sussman & Wald] 735*

E

EAR. History 428 – e
EASTER seals 429 – e
ECHINOCOCCUS. Cysts [Anglem] 341 – cr
[Welch] 827 – cr

EDITORIALS

Adoption in Massachusetts 835
Aid for disabled 470
Amending Britain's health service 156
American Heart Association. Campaign 313
American Red Cross 352
American way of life 110
"And Post O'er Land and Ocean Without Rest" 516
Annual meeting 711 – mms
Another year of decision 35
Antibiotics and blood coagulation 240
Arthritis and rheumatism 914
Atomic accidents 799
"Better to Serve" 313
Blue Cross reports 948
Bookplates. Medical 558
Boston Guild for Hard of Hearing 632
Brill's disease 386
Cancer. Give to conquer 516
Changing nature of pneumonia 155
Corti and his research 428
Council meeting Feb. 6, 312 – mms
Cross purposes 556
Crystalloid-colloid relations 633
Cui Bono 1021
District medical publications 631
Double vision 242
Easter Seal appeal 429
Education à la mode 558 – mms
Elusive virus 200
Emergency maternity and infant care 754
Epidemiology of cancer 515
Etiology of megaloureters 74
Federal Department of Health 795
(*Ex*) *Fenestra* 672
"First do no harm" 111
Fluoridation of water supply 351
Food for aged 591
Forsyth Dental Infirmary for Children 1022
Foot-and-mouth disease in Canada 755
Foundations. Stability 427
Gallupe plan 988
General Practice Clinic 385
German medical interns in United States 591
Governor's message 111
Growth of specialty 877
Harvard necrology 671
Health and wealth in old New York 714
Help for handicapped 948
Hemorrhagic fever. Epidemic 712
How firm these foundations? 427
Immunization in relation to poliomyelitis 1023
Inaudible no more (sound film) 990
Institute of Administrative Medicine 270
Internship matching plan 310
Intra-arterial transfusion 989
Japan Medical Association 756
Journal of Student American Medical Association 239
Land method of processing x-ray films 271
Let freedom ring 199
Lincoln case 514
"Little strokes" 154
Mad as a March hare. (MMS dues. Nonpayment) 352 — mms
(Tracy Burr) Mallory Memorial Fund 272
Massachusetts. New medical school 1021
"Medical Intelligence" 271
Medical Society of London 1023
Military and civilian medicine 914
Millionth victim 74
Money talks 470
Myth exploded 471
National Health Commission 72
National Medical Fellowships, Inc. 990
National Tuberculosis Association 796
New drugs for tuberculosis 797
New England's health 879
Newshawks gather 36
New therapeutic hazards 947
Norfolk South points way 201
Nursing reorganizes 878
Old drug comes of age? 429
Pesticides 37
Physician as citizen 632
Physicians' art 112
Postscriptum (Christian) 310
Prize essays. Awards 836
Progress in treatment of tuberculosis 468
Proposed new medical school in Massachusetts 946
(Isaac) Ray Medical Library at Butler Hospital 672
Red Cross Blood Program and physician 671
Retrospect and introspect 834
Roentgenologic identification of bodies 73
(Benjamin) Rush in Edinburgh 241
Salute to *Diabetes* 387
Seventh Postgraduate Lecture Course, Mar. 3–Apr. 30, 272 – mms
(Lemuel) Shattuck award 915
Support of medical education 35
Synthetic estrone 157
Token of authority (A.M.A. gavel) 714
Typhoid. Modern 835
Union health departments 350
Union of reporting secretaries 879
Vaginal smear 557
Veratrum viride 429
(De) Villiers Foundation 592
Voluntary evaluation of laboratories 388
Zodiacus Medicus 756

EMBOLISM. Pulmonary [Brailey] 745 – cr
Prevention [Wilkins & others] 360*
Recurrent. Surgery [Leonard & Cogan] 733*
ENCEPHALITIS. Postvaccinal [Bickers] 929*
Virus [Ayer] 266 – cr
EQUILIBRIUM. Disordered [J. C.] 458 – mi
EQUIPMENT wanted [Morgan] 1024 – c
ERYTHEMA multiforme bullosum [Agostas & others] 217*
ESOPHAGUS. Fistula [Mellins] 896 – mp
Tumors [Schatzki] 1015 – cr
ESTRONE. Synthetic 157 – e
EYE disease. ACTH [Wolfson & others] 474 – c

F

FEDERAL medical services [Page] 765*
FEMUR. Fractures. Nailing [Cave] 284 – ness
(WILLIAM L.) FLEMING 277 – nn
FLICKER–FUSION test [Hopkins] 401*
FLUID losses [Cooke & Crowley] 637*
FOOT-AND-MOUTH disease in Canada 755 – e
(RICHARD) FORD 390 – nn
FORSYTH DENTAL INFIRMARY FOR CHILDREN 1022 – e
FOUNDATIONS. Stability 427 – e
FUNGUS disease [Jillson & Buckley] 996*

G

GALL BLADDER. Nonvisualized [Martin & Massimiano] 488*
(HAROLD QUIMBY) GALLUPE 991 – o
GALLUPE PLAN 988 – e
[Cataldo & Riley] 992 – c
GASTROINTESTINAL tract. Foreign bodies [Persky & Frank] 223*
GENERAL PRACTICE CLINIC 385 – e
GERIATRICS 154 – e
GLOBULIN. Immune serum. Preservation 389 – mdph
GLOMERULONEPHRITIS [Crawford] 193 – cr
GLYCOSIDES. Cardiac [Feinblatt & Ferguson] 905 – mi
GÖTTINGEN. University [Morgan] 1024 – c
GOVERNMENT and physicians [Sarkisian] 594 – c
GOVERNOR'S message 111 – e
GREAT BRITAIN. Health service 156 – e
GREATER BOSTON MEDICAL SOCIETY, Jan. 16, 40; Feb. 13, 242 – n
GUAIAC stool test [Holt] 864 – mi
GUILLAIN–BARRÉ syndrome [Stillman & Ganong] 293*

COLLEGE OF AGRICULTURE AND APPLIED SCIENCE
LIBRARY
MAR 14 1952
MANHATTAN KANSAS

H

Half century of general practice [Luce] 783 – mi
(Samuel W.) Hamilton Memorial Lecture and Award 1024 – misc
Hampden District. Emergency service [Baker] 520 – c
Hampden District Medical Society, Jan. 22, 76; Apr. 22, 635 – n
(J. Leo) Hanson. (Revocation of License) [Cochrane] 757 – c
Harvard Medical Society, Jan. 15, 40; Mar. 11, 390; Apr. 22, 595 – n
Harvard necrology 671 – e
Health Departments, Union 350 – e
  Information 314 – mdph
  Organizations. Co-ordination 714 – e
  Public 714 – e
  Services. Minimum 517 – mdph
Heart. Amyloidosis [Craige] 302 – cr
  Auricular sounds [Rattigan & others] 130*
  Dilatation [Sprague] 785 – cr
  Disease. Congenital [Williams] 419 – cr
  Rheumatic [Bland] 906 – cr
  [Palmer] 190 – cr
Hemoglobinuria. Paroxysmal nocturnal [Merliss] 642*
Hemorrhagic fever. Epidemic 712 — e
Hepatitis. Viral. Complications [Leibowitz & Gorman] 932 – mp
Hepatoma [Homans] 588 – cr
Herpes Simplex. Latent 200 – e
  [Carton & Kilbourne] 172*
Herpes Zoster. Antibiotic treatment [Kass & others] 167*
(A. Bradford) Hill. Lecture, May 28, 837 – n
(William L.) Holt 38 – nn
Hormones [Lewison & Chambers] 1*
Hospitals
  Beth Israel Hospital. Medical Service, Jan. 30, 160 – n
    Refresher course 800 – n
  Boston City Hospital. Alumni Association, Apr. 26, 476 – n
    Fracture Service, Feb. 6, 114 – n
  Boston City Hospital. House Officers' Association, Feb. 5-26, 160; Mar. 18–Apr. 15, 476; Apr. 22-29, 559; May 6–June 3, 634; June 5, 760 – n
  Boston Floating Hospital, Apr. 7, 521 – n
  Boston Lying-in. Postgraduate Course 313 – e
    Postgraduate Course in Obstetrics and Pediatrics, Apr. 17-19, 315, 433 – n
  Butler Hospital 672 – e
  Children's Hospital, Apr. 17-19, 315 – n; Postgraduate Course 313 – e; 315, 433 – n
  New England Hospital, May 26, June 2, 9 and 16, 838 – n
  Postgraduate Course in Obstetrics and Pediatrics, Boston Lying-in Hospital and Children's Hospital, Apr. 17-19, 315, 433 – n
  Springfield Hospital, Feb. 2-27, 204; Mar. 1-29, 316; Apr. 2-30, 433; May 3-31, 635; June 3-28, 838 – n
  Washingtonian Hospital Institute on Alcoholism, May 20, 760 – n
Hospitals. Teaching [Wangensteen] 951*
Hundred Years Ago 37, 74, 112, 157, 202, 242, 272, 313, 353, 388, 429, 471, 517, 559, 593, 633, 673, 714, 757, 799, 836, 880, 915, 949, 900, 1024
Hunterian Society. Oration 516 – e
Hydronephrosis [Chute] 510 – cr
Hypertension 947 – e
  [Wade & Littmann] 389 – c
  Malignant [Goodman] 8*
  Treatment [Stearns & Ellis] 397*
Hyperthecosis. Ovarian [Meigs] 667 – cr
Hypertrophy [Wade & Littmann] 389 – c
Hypervitaminosis A [Naz & Edwards] 87*
"Hysteria" in Men [Robins & others] 677*

I

Ileitis. Regional. Complications [Redish] 993*
Ileum. Tumors [Donaldson] 791 – cr
Ilium. Echinococcus cysts [Anglem] 341 – cr
Immunization 1023 – e
Incontinence. Stress. Treatment [Doolittle] 364 – ness
Infant care 754 – e
Infarction. Myocardial [Clark] 233 – cr
  Myocardial [Currens] 381 – cr
Institute of Administrative Medicine 270 – e
Insulin. Dosage [Haigh & Story] 474 – c
Interamerican Congress of Cardiology, Aug. 31–Sept. 6, 522 – n
International Academy of Proctology, June 6-8, 800 – n
International College of Surgeons, Mar. 13 and 14, 354 – n
International Congress of Dietetics, July 7-11, 434 – n
International Diabetes Federation, July, 1952, 316 – n
Interns. German 591 – e
Internship 310 – e
  Matching plan [Bernstein] 594 – c
Intestines. Carcinoma [Colcock] 391 – ness
  Motility. Kymography [Chapman & others] 435*
  Obstruction [Pecora & others] 702 – mi
Intubation. Endotracheal [Beecher] 432 – c
Ischemia [Dunlop] 219 – ness

J

Japan Medical Association 756 – e
Jaundice. Methyl-testosterone. Treatment [Brick & Kyle] 176*
Jejunum. Metastasis [Starr & Miller] 250*
  Tumors [Raker] 66 – cr
Journal of Physical Medicine 757 – misc
Journalism. Medical 36 – e

K

Kappa Delta award. In orthopedic surgery 596 – n
(Chester S.) Keefer 38 – nn
Kidney. Artificial [Merrill] 17 – mp
  Calculi 633 – e
    [Butt & Hauser] 604*
  Ectopic [Stanbury] 105 – cr
  Polycystic. Congenital [Quinby] 464 – cr
  Tuberculosis [Woodruff] 69 – cr
  Tumors [Timberlake] 1017 – cr
Kingship. Britain 593 – e
Korean War. Malaria [Hall & Loomis] 90*
Kymography [Chapman & others] 435*

L

Laboratories. Approval program 388 – mdph
  Evaluation 388 – e
Lahey Clinic. Fellowship Teaching Program, Jan. 30–Mar. 26, 160 – n
(C. Guy) Lane 38 – nn
Leg ischemia [Dunlop] 219 – ness
Leiomyoma [Raker] 66 – cr
  [Schatzki] 1015 – cr
Leiomyosarcoma [Donaldson] 791 – cr
Leukemia. Surgery [Fisher & others] 477 – ness
License. Revocation. J. Leo Hanson [Cochrane] 757 – c
  Suspension. Thomas P. Beatty [Cochrane] 634 – c
  Robert B. Bigelow [Cochrane] 634 – c
Lincoln case 514 – e
Liver. Cirrhosis [Gabuzda & others] 124*
  Parenchymal disease [Mellinkoff & others] 729*
  Polyseptic. Congenital [Quinby] 464 – cr
London. Medical Society 1023 – e
Long Island College of Medicine. Alumni Day, Apr. 26, 434 – n
Low-sodium meals [Thoreson & others] 771*
Lung. Asbestosis [Arnott] 867 – cr
  Diseases [Badger] 262 – cr
  Embolism [Brailey] 745 – cr
  Function. Poliomyelitis patients [Ferris & others] 919*
  Paraffinoma [Scannell] 909 – cr
Lupus erythematosus test. Reliability [Walsh & Egan] 775*

M

Macaroni [Pecora & others] 702 – mi
Malaria. Vivax [Hall & Loomis] 90*
(Tracy Burr) Mallory 273 – o
  Memorial Fund 272 – e
Malpractice 353 – mms
Marriage. Statistics 471 – e
Massachusetts Academy of General Practice, Apr. 23, 560 – n
Massachusetts. Adoption 835 – e
Massachusetts Association of Medical Technologists, Inc., Mar 23 and May 3, 354; May 24, 800 – n

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH
Alcohol antabuse reaction [Ayres] 276
Antibiotics [MacCready] 518
Blood Banks. Licensing 836
Crippled children. Clinics, Feb. 1-28, 112; Mar. 3-28, 314; Apr. 2-30, 473; May 1-28, 673; June 2-27, 880; July 1–Aug. 25, 1024
Diseases, communicable, for Nov. 1951, 38; Dec. 203; Jan. 1952, 472; Feb. 518; Mar. 715; Apr. 880
Globulin. Immune serum. Preservation 389
Health information 314
Health services. Minimum 517
Laboratories. Approval program 388
School children. Physical examinations. Regulations 673
Tetanus antitoxin [McComb] 837
Typhoid epidemiology 472
MASSACHUSETTS HEART ASSOCIATION 315 – n
MASSACHUSETTS. Medical history [Luce] 783 – mi
Medical schools 111 – e
New medical school 946 – e; 1021 – c
MASSACHUSETTS MEDICAL SOCIETY
Annual meeting 711 – e
Applicants for fellowship 430
Council meeting, Feb. 6, 75; 312 – e; May 19, 714
Dues 633
Nonpayment. Warning 352 – e
History [Garland] 801
Ladies 673
Malpractice 353
Oration, Annual
New England Journal of Medicine. History. [Garland] 801
Postgraduate Lecture Course 558 – e
(Seventh) Postgraduate Lecture Course, Mar. 3–Apr. 30, 272 – e; program, 274; Apr. 7-16, 559; Apr. 14-24, 593; Apr. 23-30, 633
Program. One hundred and seventy-first anniversary, May 19-22, 716
Shattuck Lecture
Neurologic medicine [Denny-Brown] 839
Society meets again 913
Treasurer's office. Refund to districts 272
Treasurer's report covering refund distribution 593
Woman's Auxiliary 673
MASSACHUSETTS MEDICO-LEGAL SOCIETY, May 21, 715 – n
MASSACHUSETTS PHYSICIANS ART ASSOCIATION 112 – e
Exhibition, May 20-22, 715 – n
1. The Bride. James C. Janney 93
2. Mamie Fredericks. Fritz B. Talbot 224
3. Pansies. J. Dellinger Barney 417
4. Tar Paper House. Elizabeth Z. Kleinman 663
5. Wintertime in New England. Charles A. Lamb 794
MASSACHUSETTS PSYCHIATRIC SOCIETY, Oct. 16, 113 – misc
MASSACHUSETTS SCHOOL PHYSICIANS' ASSOCIATION, May 22, 800 – n
MASSACHUSETTS SOCIETY OF EXAMINING PHYSICIANS, May 7, 595 – n
MASSACHUSETTS TRUDEAU SOCIETY, Mar. 27, 476 – n
MATERNITY CARE 754 – e
MECKEL'S DIVERTICULUM [Nardi] 985 – cr
MEDICAL education 35 – e
MEDICAL INTELLIGENCE 271 – e
Anemia. Sickle-Cell [Sass] 583
Bone lesions. Needle biopsy [Rix & Brooks] 373 – ness
Cystitis emphysematosa [Milner & others] 902
Doctors Afield. Medicine. Ancient history [Buck] 866
Dyspnea [Palfrey] 826
Equilibrium. Disordered [C.] 458
Glycosides. Cardiac [Feinblatt & Ferguson] 905
Guaiac stool test [Holt] 864
Intestines. Obstruction. Macaroni [Pecora & others] 702
Massachusetts. Medical history [Luce] 783
Migraine. [D.] 547
Murder [Sale & Foley] 785
Physicians in art [Wiggin] 620
Pneumocholecystitis [Abel & Rousselot] 662
(Charles Scott) Sherrington [Viets] 981
Spinal-cord. Diseases [Ross & others] 823
Tendinitis. Calcific [Quigley & Renold] 1012
Trophism versus Tropism [Buck & others] 418
Tucker's wife's leg [Buck] 937
(Jan) Van Riebeeck [Viets] 503
Vein stripper [Mahorner] 340
Vitamin A. Intoxication [Reyersbach & others] 978
Volvulus [O'Malley] 744
Writing. Medical [Lee] 260
MEDICAL LIBRARIANSHIP. Congress. July, 1953 316 – n
MEDICAL SOCIETY OF LONDON 1023 – e
MEDICINE. Ancient history [Buck] 866 – mi
Jewish 472 – bml
Positions 434 – n
Progress [Christian] 281*; 310 – e
"MEGA" Syndromes [Varga & Swenson] 520 – c
MEGALOURETER 74 – e
[Swenson & others] 41*
MELANOMA. Malignant [Fanger & Roberts] 814*
MENINGIOMA [Cogan] 939 – cr
MENINGITIS. Tuberculous. Treatment [Ravreby & others] 883*
MENTAL hygiene [Seigle & others] 12*
METABOLIC diseases 390 – n
METHYL-TESTOSTERONE. Treatment [Brick & Kyle] 176*
MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY, Jan. 30, Feb. 4 and Apr. 30, 114 – n
MIGRAINE [D.] 547 – mi
MILITARY and civilian medicine 914 – e
MINNESOTA STATE MEDICAL ASSOCIATION, May 26-28, 316 – n
(WILLIAM C.) MOLONEY 390 – nn
MURDER [Sale & Foley] 785 – mi
MYASTHENIA GRAVIS [Hatch] 856*
MYELOMA [Sweet] 704 – cr
MYOCARDIAL infarction [Currens] 829 – cr

N

NARCOTIC registration 950 – n
NASOPHARYNX. Irradiation [Mueller & Flake] 924*
NATIONAL CANCER CONFERENCE, Mar. 3-5, 242 – n
NATIONAL HEALTH COMMISSION 72 – e
NATIONAL INSTITUTES OF HEALTH. Traineeships 390 – n
NATIONAL MEDICAL FELLOWSHIPS, Inc. 990 – e
NATIONAL RESEARCH COUNCIL 390 – nn
NATIONAL TUBERCULOSIS ASSOCIATION 796 – e
NECROSIS [Greenwald & others] 252*
NEPHROSCLEROSIS. Malignant [Blodgett] 345 – cr
NEPHROSIS. Lower-nephron [Partenheimer & others] 325*
NEUROBLASTOMA. Treatment [Hudson & others] 536*
NEUROLOGIC medicine [Denny-Brown] 839 – mms
NEUTROPENIA [Monto & others] 893*
NEW ENGLAND CARDIOVASCULAR SOCIETY, Feb. 4, 160; Mar. 3, 315; May 12, 720 – n
NEW ENGLAND DIABETES ASSOCIATION, Mar 21, 476; May 15, 720 – n
NEW ENGLAND HEALTH INSTITUTE, June 18-20, 760 – n
NEW ENGLAND HOSPITAL, May 26, June 2, 9 and 16, 838 – n
New England Journal of Medicine 35 – e
History [Garland] 801 – mms
Prize essay. Awards 836 – e
NEW ENGLAND PEDIATRIC SOCIETY, May 16, 676 – n
NEW ENGLAND RHEUMATISM SOCIETY, May 23, 760 – n
NEW ENGLAND ROENTGEN RAY SOCIETY. May 16, 918 – n
NEW ENGLAND SOCIETY OF ANESTHESIOLOGISTS 992 – misc; Feb. 2, 204; Mar. 1, 315; Apr. 5, 476; Apr. 8, 522; May 3, 595; May 13, 635 – n
NEW ENGLAND SOCIETY OF PHYSICAL MEDICINE, Apr 16, 595 – n
NEW ENGLAND SURGICAL SOCIETY
Aorta. Aneurysm. Treatment [Linton & Hardy] 847
Biliary-tract surgery [Hight & Lingley] 761
Bone lesions. Needle biopsy [Rix & Brooks] 375 – mi
Cancer. Surgery [Ulfelder & Meigs] 243
Carcinoma [Colcock] 391
Diverticula. Duodenal [Cattell & Mudge] 317
Dupuytren's contracture [Tanzer] 807
Femur. Fractures. Nailing [Cave] 284
Incontinence. Stress. Treatment [Doolittle] 364
Ischemia [Dunlop] 219
Rhizotomy [Munro] 161
Splenectomy [Fisher & others] 477
Surgeon and government [Mixter] 403
Ulcer. Peptic. Surgery [Lahey & Marshall] 115

NEW ENGLAND VETERANS ADMINISTRATION SURGICAL SOCIETY, May 23, 760 – n
NEW ENGLAND's health 879 – e
NEW HAMPSHIRE MEDICAL SOCIETY
Deaths
Mangurian, Armen S. 353
Metcalf, Carleton R. 353
White, Arthur W. 353
NEW YORK. Health 714 – e
NEW YORK SOCIETY FOR CIRCULATORY DISEASES, June 5, 676 – n
NEW YORK State. Medical positions 434 – n
NITROGLYCERIN test [Hopkins] 401*
NOBEL prizes 276 – bml
NORFOLK SOUTH 201 – e
NORWAY [Swank & others] 721*
NURSING 878 – e

O

OBSTETRICS [Baird] 561*
[Tenney] 613 – mp
OLD age. Hygiene 154 – e
ORTHODONTIC therapy [Swanson] 1007 – mp
OSLER SOCIETY Lecture. Visceral pain [White] 686*
OVARY. Dermoid cyst [Burgin] 424 – cr
Hyperplasia [McManus & Sommers] 890*

P

PAN-AMERICAN CONVENTION OF GASTROENTEROLOGY, May 11-17, 434 – n
PANCREAS. Carcinoma [Berg] 505 – cr
Cyst [Waddell] 942 – cr
PARATHYROID adenoma [Albright] 460 – cr
PEDIATRIC SEMINAR, Feb. 20, 280 – n
PELVIS. Cancer [Ulfelder & Meigs] 243 – ness
PENICILLIN. Sensitivity [Reiss & others] 611*
PERICARDITIS. Tuberculous [Chapman] 549 – cr
PERITONITIS. Treatment [Rutenburg & others] 52*
PESTICIDES 37 – e
PHI CHI MEDICAL FRATERNITY (DELTA CHAPTER) Apr. 16, 521 – n
PHI DELTA EPSILON FRATERNITY (BETA LAMBDA CHAPTER) Apr. 10, 559 – n
PHI DELTA EPSILON FRATERNITY (SIGMA CHAPTER) Mar 24, 316 – n
PHYSICAL examinations. School children. Regulations 673 – mdph
PHYSICIAN as citizen 632 – e
And politics [Chasen] 634 – c
PHYSICIANS' ART 112 – e
[Shull] 353 – c
[Wiggin] 620 – mi
PLAGUE. History 517 – bml
PLEURA. Effusion [Sahn & others] 927*
PNEUMOCHOLECYSTITIS [Abel & Rousselot] 662 – mi
PNEUMONIA 155 – e
Lipoid [Scannell] 909 – cr
POISONING. Mortality [Moore & others] 46*
POLIOMYELITIS [Ferris & others] 919*
Immunization 1023 – e
[Weinstein & others] 296 – mp
POSTAL rates. Change [Warren] 521 – c
(SEVENTH) POSTGRADUATE LECTURE COURSE, Mar 3–Apr. 30, 272 – e, mms; program 274 – mms; Apr. 7-16, 558 – e; 559 – mms; Apr. 14-23, 593 – mms; Apr. 23-30, 633 – mms
PREGNANCY [O'Malley] 744 – mi
Colitis [Patterson & Eytinge] 691*
Complications [Goodwin & Kenler] 572*
Toxemias [Finnerty] 646*
PRIZE. David Anderson-Berry (1953) 635 – n
Essay. Awards. *New England Journal of Medicine* 836 – e
Contest 313
PROGRESS, MEDICAL
Abdomen. Surgery [Welch] 967
ACTH [Downing] 56, 94
Asthma [Rackemann & Edwards] 815, 858
Athletics. Trauma [Thorndike] 335
Cancer. Hormonal treatment [Nathanson & Kelley] 135, 180
Cancer prevention [Wynder] 492, 538, 573
Carcinoma [Reeves] 652
Cholesterol [Thannhauser] 695
Digitalis poisoning [Cohen] 225, 254
Esophagus. Fistula [Mellins] 896
Hepatitis. Viral. Complications [Leibowitz & Gorman] 932
Kidney. Artificial [Merrill] 17
Obstetrics [Tenney] 613
Orthodontic therapy [Swanson] 1007
Poliomyelitis [Weinstein & others] 296
Radiation syndrome [Hempelmann] 776
Thyroid gland. Diseases [Cope] 368, 408, 451
Water fluoridation [Knutson] 737
PROTHROMBIN time [Holyoke & Wheelwright] 15*
PSYCHIATRIC illness [Roberts & Norton] 82*
PSYCHIATRY and medicine [Hyde] 607*
PSYCHOSOMATIC medicine [Ritchie & Guze] 75 – c
PUBLIC health. Standards 556 – e
PUBLICATIONS. Medical 834 – e
PURPURA. Thrombopenic. Antibiotic treatment [Jacobson & Sohier] 247*
PYELONEPHRITIS [Stanbury] 105 – cr
Chronic [Nussbaum & others] 289*
PYOSALPINX. Ruptured [Mixter] 553 – cr

R

RADIATION syndrome [Hempelmann] 776 – mp
(ISAAC) RAY MEDICAL LIBRARY 672 – e
RED CROSS Blood Program 671 – e
REGURGITATION. Mitral [Elkin & others] 958*
REHABILITATION 948 – e
Conference, Mar. 12, 354 – n
RESEARCH. Hospitals. Teaching [Wangensteen] 951*
RHEUMATIC FEVER. Fellowship 475 – n
RHIZOTOMY [Munro] 161 – ness
ROCKY MOUNTAIN spotted fever. Treatment [Workman & others] 962*
(BENJAMIN) RUSH 241 – e; 314 – bml

S

SARCOIDOSIS [Pittman] 305 – cr
SCHISTOSOMIASIS mansoni [Ross & others] 823 – mi
SCHOOL children. Physical examinations. Regulations 673 – mdph
Medical. New 1021 – e
SCHOOLS. Medical 111 – e
SCIENCE librarians 202 – bml
SCLEROSIS. Multiple [Swank & others] 721*
SECRETARIES. Reporting. Union 879 – e
(MIGUEL) SERVET 517 – bml
(LEMUEL) SHATTUCK award 915 – e
(CHARLES SCOTT) SHERRINGTON [Viets] 981 – mi
SHOULDER. Frozen [Quigley & Renold] 1012 – mi
SKIN diseases. Treatment [Downing] 56, 94 – mp
SOCIALIZED MEDICINE [Hunter] 277 – c
SOCIETIES
American Association of Genito-Urinary Surgeons, June 19-21, 434 – n
American Association of History of Medicine 242 – n
American College Health Association, May 1-3, 634 – n
American Electroencephalographic Society, May 10 and 11, 390 – n
American Heart Association. Campaign 313 – e
American Medical Association. Gavel 714 – e
American Neurological Association, May 8-10, 559 – n
American Psychiatric Association, Feb. 28-29, 280 – n
American Psychosomatic Society, Mar. 29 and 30, 390 – n
Boston City Hospital Alumni Association, Apr. 26, 476 – n
Boston City Hospital, House Officers' Association, Feb. 5-26, 160; Mar. 18–Apr. 15, 476; Apr. 22-29, 559; May 6–June 3, 634; June 5, 760 – n
Boston Gastroenterological Society, Mar. 26, 354 – n
Boston Society of Biologists, Feb. 13, 204; Apr. 2, 521 – n
Boston University School of Medicine Alumni Association, May 3, 560 – n
Buffalo Surgical Society 315 – nn
Greater Boston Medical Society, Jan. 16, 40; Feb. 13, 242 – n
Hampden District Medical Society, Jan. 22, 76; Apr. 22, 635 – n
Harvard Medical Society, Jan. 15, 940; Mar. 11, 390; Apr. 22, 595 – n
Japan Medical Association 756 – e

Massachusetts Association of Medical Technologists, Inc., Mar. 23 and May 3, 354; May 24, 800 – n
Massachusetts Heart Association 315 – n
Massachusetts Medico-Legal Society, May 21, 715 – n
Massachusetts Physicians Art Association. Exhibition, May 20-22, 715 – n
Massachusetts Psychiatric Society, Oct. 16, 113 – misc
Massachusetts School Physicians' Association, May 22, 800 – n
Massachusetts Society of Examining Physicians, May 7, 595 – n
Massachusetts Trudeau Society, Mar. 27, 476 – n
Middlesex South District Medical Society, Jan. 30, Feb. 4 and Apr. 30, 114 – n
Minnesota State Medical Association, May 26-28, 316 – n
National Tuberculosis Association 796 – e
New England Cardiovascular Society, Feb. 4, 160; Mar. 3, 315; May 12, 720 – n
New England Diabetes Association, Mar. 21, 476; May 15, 720 – n
New England Pediatric Society, May 16, 676 – n
New England Rheumatism Society, May 23, 760 – n
New England Roentgen Ray Society, May 16, 918 – n
New England Society of Anesthesiologists 992 – misc; Mar. 1, 315; Apr. 5, 476; Apr. 8, 522; May 3, 595; May 13, 635 – n
New England Society of Physical Medicine, Apr. 16, 595 – n
New England Veterans Administration Surgical Society, May 23, 760 – n
New York Society for Circulatory Diseases, June 5, 676 – n
Phi Chi Medical Fraternity (Delta Chapter) Apr. 16, 521 – n
Phi Delta Epsilon Fraternity (Beta Lambda Chapter) Apr. 10, 559 – n
Phi Delta Epsilon Fraternity (Sigma Chapter) Mar. 24, 316 – n
Society for Investigative Dermatology, Inc., June 7 and 8, 676 – n
South End Medical Club, Feb. 19, 242; Mar. 18, 433; Apr. 15, 595; May 13, 760; June 24, 882 – n
Tufts Medical Alumni Association, Apr. 2, 354 – n
Society for Investigative Dermatology, Inc.. June 7 and 8, 676 – n
Society meets again 913 – e
Sound film 990 – e
South End Medical Club, Feb. 19, 242; Mar. 18, 433; Apr. 15, 595; May 13, 760; June 24, 882 – n
Spasm. Control [Munro] 161 – ness
Specialism 877 – e
Spinal Cord. Diseases [Rodd & others] 824 – mi
Spleen. Metaplasia [Gardner] 621 – cr
Splenectomy [Fisher & others] 477 – ness
[Monto & others] 893*
Springfield Academy of Medicine, Jan. 8, 40; Feb. 12, 204; Mar. 11, 390; May 13, 635 – n
Springfield Hospital, Feb. 2-27, 204; Mar. 1-29, 316; Apr. 2-30, 433; May 3-31, 635; June 3-28, 838 – n
Stark unreality [Ritchie & Guze] 75 – c
State Journal Advertising Bureau 36 – e
Stockings. Elastic [Wilkins & others] 360*
Stomach. Emptying [Lolli & others] 490*
"Straw Man, Straw World" [Springer] 799 – c
Streptomycin [Shane & others] 132*
Student American Medical Association. Journal 239 – e
Surgeon and government [Mixter] 403 – ness
Surgery. Fluid losses [Cooke & Crowley] 637*
Symposium on Infant Feeding, Jan. 16, 76 – n

T

Tendinitis. Calcific [Quigley & Renold] 1012 – mi
Tennessee University 385 – e
Tetanus antitoxin [McComb] 837 – mdph
Texas Medical Center, Apr. 25 and 26, 354 – n
Thrombosis. Coronary [Balboni] 28 – cr
Hepatic [Caputi & Warthin] 1004*
Complications [Robinson] 332*
Spinal arterial [Stauffer] 30 – cr
Venous [Crane] 529*
Thyroid gland. Diseases [Cope] 368, 408, 451 – mp
Thyroiditis [McDermott] 706 – cr
Transfusion. Intra-arterial 989 – e
Reaction [Walter & others] 38 – c
Trichophyton faviforme [Jillson & Buckley] 996*
Tripelennamine [Sussman & Wald] 735*
Trophism versus Tropism [Buck] 418 — mi
Tuberculosis [Morrison & others] 329*
And brucellosis [Sharp & others] 485*
Laboratory diagnosis, Apr. 14-25 and Nov. 10-21, 354 – n
Miliary [Goodwin & Kenler] 572*
New drugs 797 – e
Symposium, July 14-18, 800 – n
Treatment 468 – e
[Shane & others] 132*
Tucker's wife's leg [Buck] 937 – mi
Tufts Medical Alumni Association, Apr. 2, 354 – n
Typhoid 835 – e
Epidemiology 472 – e
Typhus antibodies. Epidemic [Murray & others] 355*

U

Ulcer. Peptic. Surgery [Lahey & Marshall] 115 – ness
Union health-department law [Baxter] 473 – c
Union Health Departments 350 – e
[Leavell] 518 – c
[Root] 519 – c
United States Department of Health 795 – e
United States Public Health Service. Examinations 315 – n
Uremia. Nephritic [Sussman & Wald] 735*
Ureteral tonus [Redish] 993*
Uterus. Carcinoma. Radiation therapy [Reeves] 652 – mp
Rupture [Ferguson & others] 694*

V

Vaccines. Allergy [Ratner & others] 533*
Vaginal Smear 557 – e
[Lombard & others] 523*
(Jan) Van Riebeeck [Viets] 503 – mi
Vascular lesions. Cholesterol [Thannhauser] 695 – mp
Vein stripper [Mahorner] 340 – mi
Venereal-Disease Seminar, May 21 and 22, 559 – n
Veratrum viride 429 – e
[Stearns & Ellis] 397*
Vermiform appendix. Tuberculosis [Morrison & others] 329*
Vesicourethropexy [Doolittle] 364 – ness
(Henry) Viets 595 – nn
(Robert Roesler de) Villiers Foundation, Inc. 160 – n; 592 – e
Virus. Elusive 200 – e
Visceral pain [White] 686*
Vision. Double 242 – e
Vitamin A. Intoxication [Reyersbach & others] 978 – mi
Volvulus. Pregnancy [O'Malley] 744 – mi

W

(Shields) Warren 881 – nn
Washingtonian Hospital Institute on Alcoholism, May 20, 760 – n
Water. Fluoridation [Knutson] 737 – mp
Supply. Fluoridation 351 – e
Whipple's disease [Ingelfinger] 375 – cr
Windows. Hazards 672 – e
(Charles-Edward Amory) Winslow 915 – nn
Witchcraft [Springer] 799 – c
World Health Assembly 278 – misc
Wound healing. Effect of cortisone [Findlay & Howes] 597*
Writing. Medical [Lee] 260 – mi

X

X-Ray films. Processing 271 – e

Z

Zodiacus Medicus 756 – e
[Davidoff] 757 – c

AUTHOR INDEX

A

Abel, W. G. 662 – mi
Abrams, A. A. 203 – c
Adams, F. D. 102, 982 – cr
Adams, R. D. 872 – cr
Affeldt, J. E. 919*
Agostas, W. N. 217*
Albright, F. 460 – cr
Alexander, L. 46*
Amspacher, W. H. 611*
Anglem, T. J. 341 – cr
Arnott, W. M. 867 – cr
Aycock, R. R. 167*
Ayer, J. B. 266 – cr
Ayres, J. C. 276 – mdph

B

Backer, J. 721*
Badger, T. L. 262 – cr
Baird, D. 561*
Baker, J. M. 520 – c
Baker, M. P. 146 – cr
Balboni, V. G. 28 – cr
Baldwin, A. D. 771*
Bartlett, M. K. 627 – cr
Bass, H. E. 927*
Bauer, W. 205*
Baxter, R. H. 473 – c
Becker, F. B. 536*
Beecher, H. K. 432 – c
Berg, R. L. 505 – cr
Bernhard, W. G. 289*
Bernstein, B. M. 594 – c
Bickers, D. S. 929*
Bland, E. F. 906 – cr
Blodgett, F. M. 345 – cr
Blotner, H. 520 – c
Borden, C. 38 – c
Borges, F. J. 962*
Boutilier, M. 132*
Boyer, W. J. 325*
Brailey, A. G. 745 – cr
Brennan, M. J. 893*
Brick, I. B. 176*
Brooks, S. M. 375 – mi – ness
Buck, R. W. 418, 866, 937 – mi
Buckley, W. R. 996*
Burgin, L. B. 424 – cr
Burnett, J. B. 449*
Butt, A. J. 604*
Byrnes, W. W. 130*

C

C., J. 458 – mi
Campbell, J. S. 41*
Caputi, A. P. 1004*
Caron, G. H. 883*
Carton, C. A. 172*
Castagno, R. A. 12*
Cataldo, R. J. 992 – c
Cattell, R. B. 317 – ness
Cauley, J. H. 594 – c
Cave, E. F. 284 – ness
Chamberlain, J. W. 536*
Chambers, R. G. 1*
Chapman, E. M. 549 – cr
Chapman, W. P. 435*
Chasen, W. H. 634 – c
Christian, H. A. 281*
Chute, R. 510 – cr
Citron, D. S. 325*
Clark, L. D. 205*
Clark, R. J. 233 – cr
Cobb, S. 205*
Cochrane, R. C. 634, 757 – c
Cogan, D. G. 939 – cr
Cogan, M. A. 733*
Cohen, B. M. 225, 254 – mp
Cohen, M. E. 677*
Cohen, S. 355*
Colcock, B. P. 391 – ness
Contreras, A. A. 611*
Cook, C. D. 447*
Cooke, R. E. 637*
Cooper, P. 702 – mi
Cope, O. 368, 408, 451 – mp
Craige, E. 302 – cr
Crane, C. 529*
Crawford, J. D. 193 – cr
Crowley, L. G. 637*
Currens, J. H. 381, 829 – cr

D

D., L. M. 547 – mi
Dameshek, W. 477 – ness
Davidoff, R. B. 757 – c
Davidson, C. S. 124*
Denny-Brown, D. E. 839 – mms
Dexter, L. 958*
Donaldson, G. A. 791 – cr
Doolittle, L. H. 364 – ness
Downing, J. G. 56, 94 – mp
Dunlop, G. R. 219 – ness

E

Edwards, M. C. 816, 858 – mp
Edwards, W. M. 87*
Egan, R. L. 775*
Elkin, M. 958*
Ellis, D. S. 664 – cr
Ellis, L. B. 397*
Eytinge, E. J. 691*

F

Fajans, S. S. 1000*
Fanger, H. 814*
Feinblatt, T. M. 905 – mi
Ferguson, E. A. 905 – mi
Ferguson, J. H. 694*
Ferrara, M. A. 55*
Ferris, B. C., Jr. 919*
Findlay, C. W., Jr. 597*
Fine, J. 52*
Finland, M. 167*
Finnerty, F. A., Jr. 646*
Fisher, J. H. 477 – ness
Flake, C. G. 924*
Foley, J. M. 785 – mi
Frank, E. D. 223*
French, A. B. 435*
Furman, J. E. 962*

G

Gabuzda, G. J., Jr. 124*
Gardner, F. H. 621 – cr
Garland, J. 801 – mms
Garlick, W. B. 902 – mi
Ganong, W. F. 293*
Gates, O. 523*
Georgantas, V. A. 883*
Goodman, H. L. 8*
Goodwin, R. H. 572*
Gootnick, A. 252*; 277 – c
Gorman, W. F. 932 – mp
Greenberg, L. A. 490*
Greenwald, H. P. 252*
Gundersen, S. M. 449*
Guze, S. B. 75 – c

H

Haigh, G. W. 113, 474 – c
Hall, W. 38 – c
Hall, W. H. 90*
Hanelin, J. 978 – mi
Hardy, I. B., Jr. 847 – ness
Harken, D. E. 958*
Harvey, A., McG. 729*
Harwood, R. 520 – c
Hatch, H. A. 856*
Hauser, E. A. 604*
Hempelmann, L. H. 776 – mp
Hertzmark, F. 533*
Hight, D. 761 – ness
Hightower, J. A. 962*
Hoagland, H. 418 – mi
Hoffman, P. S. 435*
Holt, C. L. 864 – mi
Holyoke, J. B. 15*
Homans, J., Jr. 588 – cr
Hopkins, R. W. 401*
Horrax, G. 823 – mi
Howes, E. L. 597*
Hudson, H. W., Jr. 536*
Hunter, F. T. 277 – c
Hyde, R. W. 607*

I

Ingelfinger, F. 375 – cr
Ingraham, F. D. 568*
Ipsen, J., Jr. 46*

J

Jacob, S. W. 52*
Jacobson, B. M. 247*; 749 – cr
Jampol, J. 355*
Jaques, W. E. 41*
Jillson, O. F. 996*
Jones, C. M. 435*
Joplin, R. J. 978 – mi

K

Kass, E. H. 167*
Kelley, R. M. 135, 180 – mp
Kenler, M. D. 572*
Kilbourne, E. D. 172*
King, J. A. 252*
Knutson, J. W. 737 – mp
Kraus, H. 130*
Kyle, L. H. 176*

L

Lahey, F. H. 115 – ness
Lane, C. G. 77*
Laurie, J. H. 132*
Leavell, H. R. 518 – c
Lee, R. I. 260 – mi
Leibowitz, S. 932 – mp
Leichtling, M. 927*
Leonard, F. C. 733*
Lerman, J. 230 – cr
Lerstad, O. 721*
Lester, D. 490*
Lever, W. F. 585 – cr
Lewison, E. F. 1*
Lingley, J. R. 761 – ness
Linton, R. R. 847 – ness
Litter, J. 360*
Littmann, D. 389 – c
Lolli, G. 490*
Lombard, H. L. 523*
Loomis, G. W. 90*
Luce, D. S. 783 – mi
Luger, N. M. 252*
Luisada, A. A. 38 – c
Lundy, J. A. 444*

M

MacCready, R. A. 518 – mdph
MacMahon, H. E. 41*
Mahorner, H. 340 – mi
Mamonas, C. 902 – mi
Marble, A. 520 – c
Mardi, G. L. 985 – cr

COLLEGE OF AGRICULTURE AND APPLIED SCIENCES
LIBRARY
JAN 14 1952
MANHATTAN, KANSAS

MARSHALL, S. F. 115 – ness
MARTIN, F. 488*
MASSIMIANO, A. G. 488*
MATSON, D. D. 568*
MATTIA, V. D., JR. 289*
MCCOMB, J. W. 837 – mdph
MCDERMOTT, W. V., JR. 706 – cr
MCLAURIN, R. L. 568*
MCMANUS, R. G. 890*
MEIGS, J. V. 243 – ness; 667 – cr
MELLINKOFF, S. M. 729*
MELLINS, R. B. 896 – mp
MERLISS, R. R. 642*
MERRILL, J. P. 17 – mp
MIDDLETON, M. 523*
MILLER, G. M. 250*
MILLER, H. K. 694*
MILNER, W. A. 902 – mi
MIXTER, C. G. 329*; 553 – cr
MIXTER, G., JR. 360*
MIXTER, W. J. 403 – ness
MONTO, R. W. 893*
MOORE, M. 46*
MORGAN, A. E. 1024 – c
MORRIS, E. M. 771*
MORRIS, G. E. 366*
MORRISON, H. 329*
MUDGE, T. J. 317 – ness
MUELLER, H. L. 924*
MUNRO, D. 161 – ness
MURRAY, E. S. 355*

N

NATHANSON, I. T. 135, 180 – mp
NAZ, J. F. 87*
NICE, P. O. 485*
NICKERSON, G. H. 447*
NORCROSS, J. W. 823 – mi
NORTON, N. M. 82*
NUSSBAUM, H. E. 289*

O

OBER, W. B. 329*
OFSTROCK, A. 355*
O'MALLEY, R. C. 744 – mi

P

PAGE, R. C. 765*
PALFREY, F. W. 826 – mi
PALMER, R. S. 190 – cr
PARKER, R. T. 962*
PARTENHEIMER, R. C. 325*
PATTERSON, M. 691*
PECORA, D. 702 – mi
PEPE, ENRICO 702 – mi
PERRY, S. M. 113 – c
PERSKY, L. 223*
PHILLIPS, G. B. 124*
PITTMAN, H. S. 305 – cr
PULASKI, E. J. 611*
PURTELL, J. J. 677*

Q

QUIGLEY, T. B. 1012 – mi
QUINBY, W. C., JR. 464 – cr
QUINN, J. R. 474 – c

R

RACKEMANN, F. M. 816, 858 – mp
RAKER, J. W. 66 – cr
RATNER, B. 533*
RATTIGAN, J. P. 130*
RAVREBY, L. 883*
REBUCK, J. W. 893*
REDISH, M. H. 993*
REEVES, J. D. 652 – mp
REEVES, N. 217* – mp
REISS, E. 611*
RENOLD, A. E. 1012 – mi
REYERSBACH, G. C. 978 – mi
RILEY, C. 132*
RILEY, J. G. 992 – c
RITCHIE, J. A. 75 – c
RIX, R. R. 375 – mi – ness
ROBERTS, B. H. 82*
ROBERTS, W. F. 814*
ROBINS, E. 677*
ROBINSON, J. W. 332*
ROOT, H. F. 519 – c
ROSS, G. L. 823 – mi
ROUSSELOT, L. M. 662 – mi
RUTENBURG, A. M. 52*

S

SAHN, S. H. 927*
SALE, L. 785 – mi
SARKISIAN, S. A. 594 – c
SASS, M. 583 – mi
SAUNDERS, H. P. 203 – c
SCANNELL, J. G. 909 – cr
SCHATZKI, R. 1015 – cr
SCHLESINGER, M. J. 329*
SCHNAP, I. 12*
SCHNEIDER, G. T. 694*
SCHNITKER, M. A. 315 – c
SCHWEINBURG, F. B. 52*
SEIGLE, S. P. 12*
SELTSER, R. 296 – mp
SHAFER, H. C. 893*
SHANE, S. J. 132*
SHANKS, E. D., JR. 217*
SHARP, J. T. 485*
SHELOKOV, A. 296 – mp
SHULL, H. H. 353 – c
SIEGEL, A. C. 447*
SISE, H. S. 130*
SMITH, R. W. 474 – c
SNYDER, J. C. 355*
SOHIER, W. D. 247*
SOMMERS, S. C. 890*
SOSMAN, M. C. 958*
SPRAGUE, H. B. 785 – cr
SPRINGER, A. L. 799 – c
STANBURY, J. B. 105 – cr
STANTON, J. R. 360*
STARR, A. 250*
STAUFFER, R. 30 – cr
STEARNS, N. S. 397*
STEFFENSEN, E. H. 474 – c
STILLMAN, J. S. 293*
STORY, R. D. 474 – c
STRØM, A. 721*
SUSSMAN, R. M. 735*
SWANK, R. L. 721*
SWANSON, L. T. 1007 – mp
SWEET, W. H. 704 – cr
SWENSON, O. 41*; 520 – c
SYDENSTRICKER, V. P. 217*

T

TANZER, R. C. 807 – ness
TENNEY, B., JR. 613 – mp
THANNHAUSER, S. J. 695 – mp
THORESON, P. A. 771*
THORNDIKE, A. 335 – mp
TIMBERLAKE, W. H. 1017 – cr
TUMULTY, P. A. 729*

U

ULFELDER, H. 243 – ness
UNTRACHT, S. 533*

V

VARGA, C. 520 – c
VIETS, H. R. 503, 981 – mi

W

WADDELL, W. R. 942 – cr
WADE, L. 389 – c
WALD, N. 735*
WALSH, J. R. 775*
WALTER, C. W. 38 – c
WANGENSTEEN, O. H. 951*
WARREN, S. 521 – c; 523*
WARTHIN, T. A. 1004*
WEINSTEIN, L. 296 – mp
WELCH, C. E. 827 – cr; 967 – mp
WELCH, C. S. 477 – ness
WHEELER, E. O. 151 – cr
WHEELWRIGHT, H. J., JR. 15, 485
WHITE, J. C. 686*
WHITTENBERGER, J. L. 919*
WIGGIN, S. C. 620 — mi
WILKINS, R. W. 360*
WILLIAMS, C. 419 – cr
WINCHELL, G. D. 296 – mp
WOLFSON, W. Q. 474 – c; 1000*
WOODRUFF, L. M. 69 – cr
WORKMAN, J. B. 962*
WYNDER, E. L. 492, 538, 573 – mp

Z

ZUKEL, W. J. 771*